NIEHS National Institute of Environmental Health Sciences

Environmental Factor

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July 2011

NIEHS Spotlight

Rider honored by U.S. Public Health Service medical officers Video

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NIH honors Kunkel as distinguished investigator

In early June, NIH announced its approval for the promotion of NIEHS Principal Investigator Thomas A. Kunkel, Ph.D., to the rank of NIH Distinguished Investigator.

Annual Ethics Day probes, triggers interest Video

The NIEHS Office of Ethics continued where it left off the previous year, with a program featuring three notable speakers May 25 for the second annual Ethics Day.

Collman inspires Stony Brook graduates

NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D., welcomed from the academic ranks a new generation of future leaders in public health.

Science Notebook

Duke researcher gives 2011 Rodbell Lecture Video

Brigid Hogan, Ph.D., studies lung development in embryonic mice, and hopes her work will lead to a better understanding of the process of lung development.

Steady progress reported at SACATM

There was much to discuss and digest at this year's meeting of he Scientific Advisory Committee on Alternative Toxicological Methods June 16-17 in Arlington, Va.

T cells take center stage at NIEHS symposium

Attended by more than 100 researchers, the symposium was organized by Donald Cook, Ph.D., NIEHS principal investigator and head of the Immunogenetics Group.

Autoimmune mysteries spark ongoing research

NIEHS epidemiologist Christine Parks, Ph.D., spoke May 27 on "Autoimmune diseases: What we know (and don't know) about environmental risk factors and why we care."

Is spit the future in diagnosis of preclinical Parkinson's?

NIEHS grantee Jing Zhang, M.D., Ph.D., is a scientist on a journey, searching for the Holy Grail of biomarkers for early detection of Parkinson's disease.

NIEHS Spotlight

National conversation on public health and chemical exposures releases highly anticipated Action Agenda

The Action Agenda released June 9 outlined 48 recommendations for protecting the American public from exposure to toxic chemicals and other hazardous materials.

Austin is new NIEHS associate director for management

Austin will serve as the principal advisor to NIEHS/NTP Director Linda Birnbaum, Ph.D., on all management issues affecting the Institute.

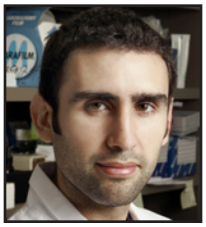
NIEHS grantee honored for new video on breast cancer research

Video

NIEHS-funded Bay Area Breast Cancer and the Environment Research Center was recently presented with the esteemed “Award of Distinction.”

Miller welcomes and challenges 2011 summer interns

Nearly every one of the 50 students participating in the 2011 NIEHS Summer Internship Program attended a talk June 16 by Acting Scientific Director David Miller, Ph.D.



NIEHS fellow receives Endocrine Society Presidential Poster Award

NIEHS visiting fellow Javier Revollo, Ph.D., received the Presidential Poster Award at ENDO Expo 2011: The 93d Annual Meeting of the Endocrine Society.

Science Notebook

Copeland chairs mitochondrial disease symposium

NIEHS has teamed up with the United Mitochondrial Disease Foundation to showcase research about mitochondrial toxicity to researchers, clinicians, and patients.

Superfund postdoc unravels arsenic exposure

Video

Arsenic exposure does not have to be in large doses in order to have severe damaging effects on a biological system, according to Courtney Kozul-Horvath, Ph.D.

NIEHS at Society for In Vitro Biology meeting

NIEHS scientists contributed their bioinformatics expertise to a weeklong annual meeting of the Society for In Vitro Biology June 4-8 in Raleigh.

NIEHS trainee wows Science Café audience

Postdoctoral fellow Jeffrey Stumpf, Ph.D., presented an engaging introduction to DNA before a capacity audience at Raleigh’s latest Science Café June 22.

Paper from Dudek group highlighted by Faculty of 1000

The study, which details the mechanism underlying rapid transcription of immediate early genes in neurons, appeared online in the journal Nature Neuroscience in May.

NIEHS nano consortium meets for progress updates

The NIEHS Centers for Nanotechnology Health Implications Research Consortium Meeting offered an opportunity for grantees to share and integrate data.

NIEHS Spotlight

Suk honored by combustion emissions group

NIEHS Superfund Research Program founder and Director Bill Suk, Ph.D., was recognized with the Adel Sarofim Award for Excellence in Combustion Research.

NIEHS partner honored for environmental stewardship

NIEHS Public Interest Partners member Mary Lamielle received the Public Service Enterprise Group Environmental Stewardship Governor's Jefferson Award.

Klotz departs NIEHS for position at Sanford-Burnham

Klotz served as director of the NIEHS Office of Fellows' Career Development part time starting in May 2007, before transitioning into a full-time role in September 2007.

Local students energized by climate change workshop Video

Durham County, N.C. students spent an exciting week with NIEHS and EPA staff, learning about the science behind climate change and related health effects.

NIEHS recognized for composting

NIEHS scored an organization honorable mention in the Environmental Stewardship category of the FY2010 HHS Green Champions Awards Program.

Henry organizes session for "Sustainable Remediation 2011"

NIEHS Health Scientist Administrator Heather Henry, Ph.D., organized a multi-agency session on "Human Health" for a green chemistry meeting June 1-3 in Amherst, Mass.

Science Notebook

NIEHS-funded study suggests high infant exposure to flame retardants Video

A new NIEHS-funded study finds infants are being exposed to chemical flame retardants found in up to eighty percent of commonly used baby products, including car seats.

This month in EHP

The Focus feature story of the July EHP examines the chemical aftermath following the March 2011 Tohoku earthquake and tsunami.

Extramural Research

Extramural papers of the month

- Prenatal PAH exposure linked to behavioral problems in kids
- Breakfast helps to reduce childhood lead poisoning
- Endoplasmic reticulum stress in obesity
- Astrocytes and microglia display distinct sensitivities to methylmercury

Intramural Research

Intramural papers of the month

- Diet may protect against mutagens in fried meat
- Formation and repair of double strand breaks in yeast
- Crystal structure-based mutagenesis of EndA nuclease
- A novel protective role for beta2 adrenergic receptor in Parkinson's disease

Inside the Institute

Representative David Price holds town hall at NIEHS

Veteran Congressman David Price, D-N.C., was back in his district June 17 to address NIEHS employees and contractors at a community forum in Rodbell Auditorium.

"Going local" at the spring Farmers' Fair

Local farmers and crafters exhibited their produce and products June 15 on the patio outside the Rall Building as part of the NIEHS spring Farmers' Fair.

Calendar of Upcoming Events

- **July 1**, in Rall F-193, 1:00-3:00 p.m. — Grace Kissling, Ph.D., presents session one of the Biostatistics Short Course. The series continues **July 5**, in Rall F-193, 1:00-3:00 p.m., with Shyamal Peddada, Ph.D., presenting Biostatistics session two; **July 6**, in Rall F-193, 12:30-2:00 p.m., with Keith Shockley, Ph.D., presenting Bioinformatics Short Course session one; **July 7**, in Rodbell C, 10:00 a.m.-12:00 p.m., with Tom Randall, Ph.D., presenting Bioinformatics session two; and **July 8**, in Rall F-193, 1:00-3:00 p.m., with Robnet Kerns, Ph.D., presenting Bioinformatics session three.
- **July 5**, in Rall Executive Conference Room, 12:00-1:00 p.m. — Receptor Mechanisms Discussion Group, with Howard Rockman, M.D., discussing "Biased GPCR [G protein-coupled receptor] Signaling"
- **July 6**, in Rodbell Auditorium, 3:30-4:30 p.m. — Laboratory of Reproductive and Developmental Toxicology Seminar Series presentation on "Development of Polymeric Nanoconjugates for Cancer Targeting and Therapy," by Jianjun Cheng, Ph.D.
- **July 7**, in Rodbell Auditorium, 10:00-11:30 a.m. — Summer Internship Program Seminar Series, featuring Stavros Garanziotis, M.D., discussing respiratory biology research
- **July 14**, in Rodbell Auditorium, 10:00-11:30 a.m. — Summer Internship Program Seminar Series, featuring Patricia Jensen, Ph.D., discussing neurobiology research
- **July 14**, in Rodbell Auditorium, 3:00-4:00 p.m. — Superfund Research Program Distinguished Lecture Series, featuring Bernhard Hennig, Ph.D., addressing "PCBs, Nutrition and Endothelial Cell Function: Implications in Atherosclerosis"
- **July 15 (off-site event)**, at the NIH Natcher Center, Bethesda, Md., 8:00 a.m.-4:00 p.m. — Partnerships for Environmental Public Health (PEPH) Workshop #1 - Environmental Health Communication: Methods, Research, and Training
- **July 18-20**, in Rodbell Auditorium, 8:30 a.m.-5:30 p.m. — Outstanding New Environmental Scientists (ONES) Grantee Meeting
- **July 28**, in Rodbell Auditorium and Rall Mall, 9:00 a.m.-12:00 p.m. — Summer Internship Program Poster Session
- View More Events: NIEHS Public Calendar

NIEHS Spotlight

Rider honored by U.S. Public Health Service medical officers

By Eddy Ball

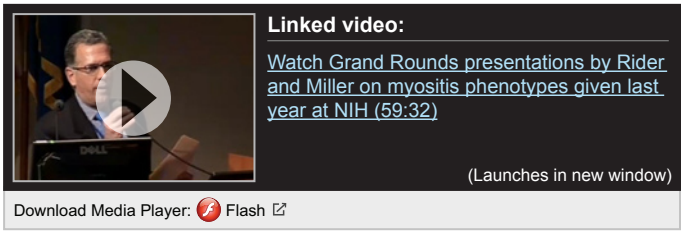
As modest as she is talented, hardworking, and dedicated, NIEHS physician-scientist and clinical researcher Captain (Capt.) Lisa Rider, M.D., is quick to acknowledge the help of others in shaping her professional achievements. Among those milestones is her selection as 2011 Physician Researcher of the Year by the Physicians Professional Advisory Committee (PPAC) of the United States Public Health Service (USPHS), which represents the nearly 900 medical officers in the more than 6,000-member Corps.

Rider, right, was joined by Miller, left, and former U.S. Surgeon General Richard Carmona, M.D., at her most recent promotion ceremony in 2005. (Photo courtesy of Lisa Rider)

When the PPAC notified her of its intention to honor her, Rider acted characteristically by pointing out the important contributions to her career by her colleague and mentor in the Environmental Autoimmunity Group (EAG) based in Bethesda, Md., Principal Investigator and fellow USPHS commissioned officer, Capt. Fred Miller, M.D., Ph.D.

"I am extremely honored and humbled to receive this recognition by the Public Health Service," Rider said. "I greatly appreciate all of the support, guidance, and wisdom that Fred Miller has provided through much of my career, and also to NIEHS for a climate that promotes our mission of improving the public health through scientific advances."

Rider, who is deputy chief of the EAG and an officer in the Commissioned Corps of the USPHS, received her award June 21 at the annual meeting of the USPHS Officers Association, the 2011 USPHS Scientific and Training Symposium, in New Orleans. She was singled out for her groundbreaking research in the area of a mysterious and debilitating autoimmune disease among children, a condition thought to be triggered by environmental exposures and genetic polymorphisms.



Combining basic and clinical research

"[This award is] presented in recognition of her noteworthy basic and clinical research into juvenile dermatomyositis," read the citation on her plaque. "Her leadership in epidemiologic and clinical studies has contributed substantially to public health practice. Her career achievements are in the highest tradition of the United States Public Health Service."

Rider is one of the leading authorities on clinical presentations, pathogenesis, and treatment of idiopathic inflammatory myopathies, particularly the childhood forms of these diseases. She is first author with Miller on a milestone publication released earlier this year in the Clinician's Corner of the high-impact Journal of the American Medical Association (JAMA).

In its recommendations to clinicians and researchers, the paper presented a compelling argument for systematically categorizing heterogeneous myositis syndromes into mutually exclusive and stable phenotypes by using clinical and immune response features of the myositis syndromes.

Rider's award is one of three presented to senior USPHS medical officers each year, honoring clinicians, researchers, and applied public health executives. Two additional awards recognize the achievements of junior officers and inactive Reserve Corps physicians.

Shown at the awards ceremony June 20 are, left to right, Chief of Staff to the Surgeon General R.Adm. Christopher Halliday, D.D.S.; Chief Professional Officer R.Adm. Clare Helminiak, M.D.; Rider with Research Physician of the Year plaque; Cmdr. Meena Vythilingam, M.D., with Applied Public Health Physician of the Year plaque, Cmdr. Michael Truesdell, M.D., with Clinical Physician of the Year plaque; Lt. Cmdr. Ezra Barzilay, M.D., with Junior Physician of the Year plaque; and Deputy Surgeon General R.Adm. Boris Lushniak, M.D. (Photo courtesy of Paul Jung)

USPHS researchers and clinicians at NIEHS

Along with Rider and Miller, USPHS commissioned officers play important roles as scientific administrators, researchers, and clinicians working at the Research Triangle Park, N.C., headquarters of NIEHS. They are part of the 103 USPHS physicians and the total 328 USPHS commissioned officers working at NIH in all categories.

Commander (Cmdr.) Paul Jung, M.D., serves as chief of staff in the Office of the Director; Capt. Aubrey Miller, M.D., is NIEHS chief medical officer; and Rear Admiral (R.Adm.) William Stokes, D.V.M, is director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). Diane Forsythe, D.V.M., chief of the Comparative Medicine Branch, and Deputy Chief Mary Grant, V.M.D., are retired commissioned officers.

Principal Investigators Capt. Matt Longnecker, M.D., Sc.D., and Capt. Jack Taylor, M.D., Ph.D., are heads of Epidemiology Branch research groups at NIEHS. Taylor has a dual appointment in the Laboratory of Molecular Carcinogenesis. Epidemiology Branch Principal Investigators Allen Wilcox, M.D., Ph.D., and Walter Rogan, M.D., are retired commissioned officers.

On the clinical front, Lieutenant (Lt.) Cmdr. Lindia Engram is an occupational health nurse in the NIEHS Health and Safety Branch, Cmdr. Debra King is a medical technologist in the NTP Clinical Pathology Group, and Lt. Cmdr. John McLamb is a health physicist in the NIEHS Health and Safety Branch.

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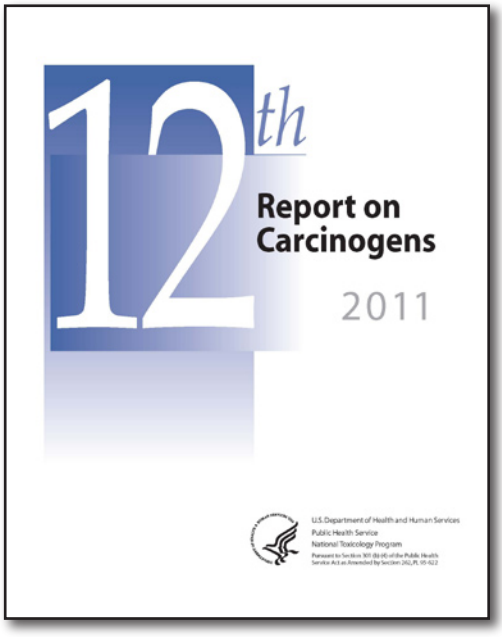
New substances added to HHS Report on Carcinogens

By Robin Mackar

The U.S. Department of Health and Human Services added eight substances to its latest Report on Carcinogens, a science-based document that identifies chemicals and biological agents that may put people at increased risk for cancer. The report was officially announced by NIEHS during a press briefing June 10.



The industrial chemical formaldehyde and a botanical known as aristolochic acids are listed as known human carcinogens. Six other substances — captafol, cobalt-tungsten carbide (in powder or hard metal form), certain inhalable glass wool fibers, o-nitrotoluene, riddelliine, and styrene — were added as substances that are reasonably anticipated to be human carcinogens. With these additions, the 12th Report on Carcinogens now includes 240 listings.

"Reducing exposure to cancer-causing agents is something we all want, and the Report on Carcinogens provides important information on substances that pose a cancer risk," said Linda Birnbaum, Ph.D., NIEHS/NTP director. "The NTP is pleased to be able to compile this report."

John Bucher, Ph.D., associate director of the NTP added, "This report underscores the critical connection between our nation's health and what's in our environment."

The Report on Carcinogens is a congressionally mandated document that is prepared for the HHS Secretary by the NTP. The report identifies agents, substances, mixtures, or exposures in two categories — known to be a human carcinogen and reasonably anticipated to be a human carcinogen. A listing in the Report on Carcinogens does not by itself mean that a substance will cause cancer. Many factors, including the amount and duration of exposure, and an individual's susceptibility to a substance, affect whether a person will develop cancer.

Once a substance is nominated by the public or private sector and selected for consideration, it undergoes an extensive evaluation with numerous opportunities for scientific and public input. There were at least six opportunities for public input on each substance. The NTP used established criteria to evaluate the scientific evidence on each candidate substance under review. The NTP drew upon the scientific expertise of several federal agencies, including the National Institutes of Health, Centers for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry, U.S. Food and Drug Administration, U.S. Environmental Protection Agency, U.S. Consumer Product Safety Commission, and Occupational Safety and Health Administration.

"The strength of this report lies in the rigorous scientific review process," said Ruth Lunn, Dr.P.H., director of the NTP Office of the Report on Carcinogens. "We could not have completed this report without the significant input we received from the public, industry, academia, and other government agencies."

A detailed description of each substance listed in the Report on Carcinogens is included in the new report. NTP has posted the report and other materials, such as fact sheets and frequently asked questions, online.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison.)

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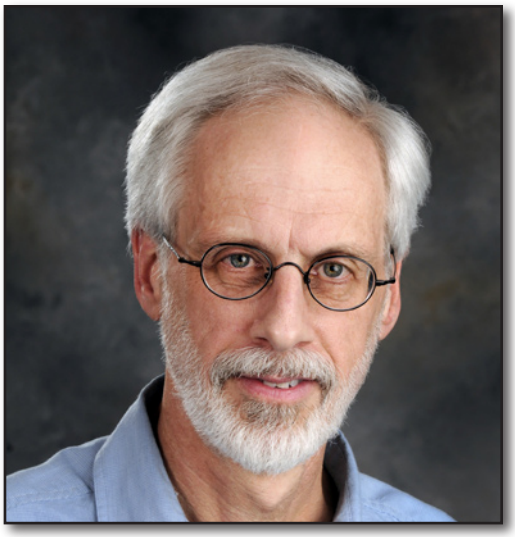
Birnbaum is first board-certified toxicologist to head NIEHS. (Photo courtesy of Steve McCaw)



NTP Associate Director Bucher (Photo courtesy of Steve McCaw)

Director of the NTP Office of the Report on Carcinogens Lunn joined NIEHS in 2008. (Photo courtesy of Steve McCaw)

NIH honors Kunkel as distinguished investigator

By Eddy Ball

NIH announced in early June its approval for the promotion of NIEHS Principal Investigator Thomas A. Kunkel, Ph.D., to the rank of NIH Distinguished Investigator, one of the highest honors NIH awards to its scientists. The promotion, which only an estimated two to three percent of NIH scientists ever achieve, requires a special peer review and approval by the director of NIH.

As the memo from NIH Director Francis Collins, M.D., Ph.D., explains, "This title is reserved for tenured intramural senior investigators who are at the highest level of accomplishment in their respective fields." Following a nomination by NIEHS/NTP Director Linda Birnbaum, Ph.D., a peer review of Kunkel's performance was conducted by the special NIH Distinguished Investigator Review Subcommittee prior to approval by Collins.

Kunkel has developed several novel experimental approaches for investigating DNA replication, and he is considered one of the world's leading experts in the field. A recent review of the Laboratory of Structural Biology said of Kunkel, "He is considered to be one of the major intellectual drivers of the laboratory and also possesses excellent managerial skills." (Photo courtesy of Steve McCaw)

Molecular genetics and structural biology

Along with directing the NIEHS Environmental Biology Program, Kunkel serves as head of the Laboratory of Molecular Genetics DNA Replication Fidelity Group and chief of the Laboratory of Structural Biology. This dual appointment reflects one of the qualities that make his research stand out in the field — the forging of a bond between molecular genetics and structural biology. One of his recent papers, for example, used this cross-specialty approach to uncover strong evidence to support Watson and Crick's theory about the origin of spontaneous base substitution mutations, a theory previously unproven in the more than half century since its proposal in 1953 (see story).

In his work on DNA replication fidelity, Kunkel's authorship is frequently associated with firsts in the understanding of the DNA transactions that determine DNA replication fidelity. He is a major contributor to new knowledge about the several repair processes that operate prior to DNA replication to remove the many types of DNA damage generated by endogenous cellular metabolism or exposure to the environment.

Three decades of outstanding research

During his almost 30-year tenure at NIEHS, Kunkel has published numerous peer-reviewed articles in leading scientific journals, as well as several book chapters, and mentored a number of distinguished scientists in his lab. He has authored or coauthored numerous outstanding studies recognized as NIEHS Intramural Papers of the Month and has published 138 articles in rigorously peer-reviewed, high-impact journals in the past decade alone.

In addition to honors from professional organizations, Kunkel was selected as NIEHS Scientist of the Year in 2005, and won Paper of the Year in 2004, 2007, 2008, and 2009. When the NIH celebrated scientific discoveries made at the NIH over the previous two decades, among the 20 most cited papers by NIH investigators were two authored by him.

Among Kunkel's many honors include his selection as chair of several Gordon Research Conferences, an Environmental Mutagen Society Award for Basic Research, and the Mutation Research Award. He received an honorary doctoral degree from Umeå University in 2007 for his identification of the DNA polymerase that replicates the leading strand of the eukaryotic nuclear genome.

Kunkel has presented a number of invited distinguished lectures and served as chair at numerous professional symposia and meetings, as well as national search committees and tenure committees. He has considerable editorial expertise, having served for 15 years on the editorial board of the Journal of Biological Chemistry and for the past eight years as an editor for DNA Repair. He performs peer-review for numerous journals, and his advice is frequently sought for grant reviews.

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Annual Ethics Day probes, triggers interest

By Josh Zeldin

The NIEHS Office of Ethics continued where it left off the previous year, with a program featuring three notable speakers for the second annual Ethics Day, May 25 in Rodbell Auditorium (see story). Organized by Bruce Androphy, J.D., director of the Office of Ethics and deputy ethics counselor, the event attracted NIEHS employees and guests, including several visitors from the National Human Genome Research Institute.

The underlying goal of Ethics Day was to provide an open forum for discussing ethics in the work place, with special emphasis on biomedical research, and providing ample opportunity for questions and comments about regulatory paperwork and forms, ambiguous research scenarios, and the line between official and outside activities. The speakers promoted healthy and at times probing discussions of how to avoid unethical conduct in the future as well as tackle any current issues.

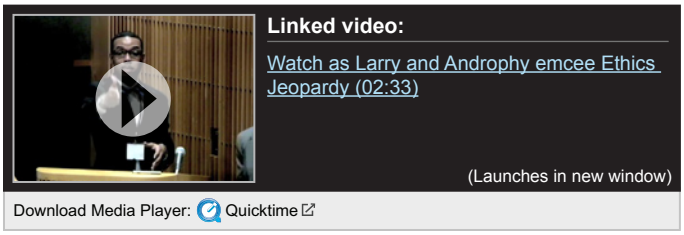
Birnbaum welcomed members of the audience and told listeners, "I think you know I am committed to a strong ethics program." (Photo courtesy of Steve McCaw)

Separating official and private activities

Kicking off the presentations was Patrick Shepherd, a training specialist at the U.S. Office of Government Ethics. After welcome remarks by NIEHS/NTP Director Linda Birnbaum, Ph.D., and an introduction by NIEHS Ethics Coordinator Jackie Stillwell, Shepherd opened his presentation with a discussion of the sometimes subtle distinctions between official work duties and outside activities that could possibly be or even appear to be of ethical concern.

The presentation led to questions from the audience, many about the sometimes burdensome paperwork involved in disclosing outside activities and the limitations they experience interacting professionally with people outside the government. Shepherd acknowledged the concerns of some attendees and assured the audience, "We're looking for ways you can do that within the rules."

Offering the audience an opportunity for active participation, the next activity of the day involved a lighthearted Ethics Jeopardy competition, with attendees split into four teams. Directed by North Carolina Central University law student Tomasi Larry, the competition generated a stimulating discussion of ethical topics both within teams and between competing teams. Categories included Prohibited Gifts, Ethics Basics, Bioethics, and Movies and Books.



Shepherd emphasized a message that NIEHS employees have heard many times from Androphy and others in the Office of Ethics: Take the time to ask about situations and activities that could be perceived as crossing the line between official and personal. (Photo courtesy of Steve McCaw)

The lessons of New York's Troopergate

Following a short break, attendees gathered for a lunchtime presentation by Meave Tooher, J.D., an attorney who formerly worked with Androphy at the New York State Commission on Public Integrity. Tooher discussed the commission's investigation into the scandal surrounding Elliot Spitzer in 2007, dubbed "Troopergate" by the New York media, although the name has since become more widely associated with a scandal in Alaska the following year. Central to Tooher's story was the persistence of investigators who worked their way through thousands of e-mails and confidential documents they obtained from often-reluctant sources.

Relating these practices concerning confidentiality to the NIEHS workplace, Tooher observed, "Email is one of the most dangerous vehicles out there… [and] you have to assume that e-mail is going to be read by the world." Tooher warned employees to be cautious in handling classified documents. She also stressed the importance of seeking guidance and advice if uncertainty arises and of speaking up when something seems unethical. "If you know someone is doing the wrong thing, it is incumbent to bring it to their attention."

Contractor Fanny Augustin, left, and Robin Jones enjoy one of the lighter moments of Shepherd's discussion. (Photo courtesy of Steve McCaw)

Assessing the social value of biomedical research

The final event of the day was a presentation by Franklin Miller, Ph.D., senior faculty in the Department of Bioethics at NIH. Miller's presentation sparked a lively discussion among attendees about the definition of research coercion of human subjects and how to assess the potential social value of research that could possibly harm participants. Miller urged attendees to appreciate the ambiguity associated with medical ethics and underscored the importance of such issues as the risk of mortality in research and compensation for research participation.

Miller cautioned his listeners that they might find more questions than answers in their quest. “Bad things do happen in unpredictable ways,” Miller argued, “but just because it [a clinical trial] turned out bad doesn’t mean it was unethical.”

(Josh Zeldin is a summer intern with the NIEHS Office of Communications and Public Liaison. He is a student at the University of North Carolina at Chapel Hill.)

Most of the audience, including NIEHS Deputy Director Rick Woychik, Ph.D., joined in the merriment. That afternoon, Woychik introduced Miller and helped moderate the animated question and answer session. (Photo courtesy of Steve McCaw)

As Larry, right, emcees Ethics Jeopardy, Androphy laughs along with the audience. (Photo courtesy of Steve McCaw)

As she described the resistance she encountered during New York’s Troopergate, Tooher’s demeanor reflected the seriousness of her struggles with politicians and political appointees. (Photo courtesy of Steve McCaw)

Miller, left, talked afterwards with his counterpart at NIEHS, Bioethicist David Resnik, J.D., Ph.D. (Photo courtesy of Steve McCaw)

Office of Ethics staffers have reason to smile after holding the second annual Ethics Day at NIEHS. Shown, left to right, are Stephen Copeland, Patricia Harris, D.J. Joya, Stillwell, and Androphy. (Photo courtesy of Steve McCaw)

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Collman inspires Stony Brook graduates

By Ed Kang

NIEHS Division of Extramural Research and Training Director Gwen Collman, Ph.D., welcomed from the academic ranks a new generation of future leaders in public health. For the 125 conferees, faculty, and esteemed guests of the Graduate Program in Public Health at Stony Brook University, Collman's keynote address May 24 reflected on her study of environmental risk factors for breast cancer on Long Island and how those challenges helped shape the landscape for future population research.

The lessons of Long Island

Karen Miller, a founder of Huntington Breast Cancer Action Coalition and member of the NIEHS Public Interest Partners group, introduced Collman as a valued partner to the university — one with deep ties to Long Island. Indeed, in her former role as NIEHS program administrator, Collman spent a decade, beginning in the mid-1990s, looking at environmental causes of breast cancer among Long Island women. In her commencement speech, she spoke inspiringly of the lessons learned from the 10 years she, and many others, spent trying to decipher the causes of what was perceived as a cancer hot spot.

One of those lessons was the recognition of community relationships in the research process. "Community connections are an integral part of the research process, and their concerns about environmental hazards in

their neighborhoods, and how it affects their health and the health of their children, are paramount. These relationships really make or break a study," Collman explained.

"Some of the most interesting times were when community members took me in their cars, or on walks to show me what their neighborhoods look like and what they are dealing with." These "toxic tours" as Collman called them, can sometimes have a game-changing effect.

But, Collman also noted how anxious the Long Island community was to have research point to a definitive cause for why breast cancer was seemingly so prevalent. "We had to plan for that by having a shared understanding between scientists and the participants, to understand what research really means and what can be found and what can't. We won't have all the answers when we want them, but we can keep working towards answers."

Collman joked that it was her mother's desire for her to attend Stony Brook — just a short train ride away from her home — that helped her make the decision to seek an undergraduate degree from Binghamton. "But her wish that I participate in commencement at Stony Brook finally came to fruition," Collman quipped. (Photo courtesy of Melissa Mastrogiovanni)

According to Collman, the women of the community eventually saw the Long Island Breast Cancer Study as a national resource – the beginning of a relationship with the government, and an investment and commitment to continue to work on these problems. Other research has used the Long Island work as a springboard, and Collman credits the study as an evolutionary influence in current translational research, where community tie-in is integral.

Opportunities abound for new graduates

The final lesson offered to the graduates was one of perspective on the question of "What's next?" — a concern many in the audience were sharing as they transition from academia to the professional ranks. Collman was quick to paint a positive employment picture for graduates. "It takes many types of scientists, in many discipline areas, to unravel the clues of complex diseases. That's where you come in," she comforted. "Whether you work in scientific, regulatory, public policy formation or the health communication side of public health, you have the best new methods and technologies at your disposal."

Closing out the day for graduates, Collman concluded her talk with a challenge to those on the verge of new careers: "Be bold and reach out to the communities which you will serve. Your work will be richer for it, the discoveries will be more relevant, and the messages will be clearer because of the dialog which you initiated."

Visit culminates with Alda meeting

Collman's recent visit to the campus of Stony Brook University included several stops to network with faculty from various departments.

Accompanied by Miller, Collman met with faculty from the Consortium for Inter-Disciplinary Environmental Research (CIDER). This initiative brings together faculty from diverse disciplines to create synergistic collaborations that address large, complex environmental issues. The participants in CIDER are associated with departments in Arts and Sciences, Engineering, the School of Medicine, and the School of Marine and Atmospheric Sciences.

Collman also spent time with the Center for Communicating Science, a program that seeks to train the next generation of scientists and health professionals to communicate more effectively with the public. In addition to the dean and members of the center, Collman spoke via Skype with famed actor and faculty member, Alan Alda, to discuss their shared passion for communicating science.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

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National conversation on public health and chemical exposures releases highly anticipated Action Agenda

By Ian Thomas

The National Conversation on Public Health and Chemical Exposures released its highly anticipated comprehensive Action Agenda June 9, outlining 48 recommendations for protecting the American public from exposure to toxic chemicals and other hazardous materials.

Balbus has participated in the Conversation in his role as Leadership Council representative and chair of the Monitoring Work Group. (Photo courtesy of Steve McCaw)

As the culmination of a two-year joint effort between an array of nonprofit and industry organizations, the general public, and various government agencies, including NIEHS, this agenda identifies potential risks to public health and explores possible solutions in areas like policy reform, chemical exposure prevention and the promotion of children's health.

"Scientists from across NIEHS gave their time and input to the National Conversation on Public Health and Chemical Exposures, helping to create a rich and thoughtful set of recommendations to move the country forward on chemicals management and safety," explained John Balbus, M.D., senior advisor for public health and one of several NIEHS contributors to the report. Others included Jean Harry, Ph.D., Liam O'Fallon, Fred Miller, M.D., Ph.D., and Beth Anderson (see related story for details).

Portier has been a participant in the Conversation since its kickoff meeting in 2009. (Photo courtesy of Steve McCaw)

"The National Conversation was grounded in the vision of a nation that uses and manages chemicals in ways that are safe and healthy for all people," added Chris Portier, Ph.D., director for the National Center for Environmental Health and Agency for Toxic Substances and Disease Registry at the Centers for Disease Control and Prevention, a fellow participant in the Conversation initiative. "This vision grows out of the nation's rising awareness that human health and the environment are deeply intertwined." Portier was a former NIEHS senior advisor.

For more information regarding the report and its recommendations, visit the National Conversation Web site.

(Ian Thomas is a writer/editor in the NIEHS Office of Communications and Public Liaison)

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Austin is new NIEHS associate director for management

By Eddy Ball

NIEHS welcomed Joellen Harper Austin as its new associate director for management and executive officer June 20 at its Research Triangle Park, N.C. headquarters. She will serve as the principal advisor to NIEHS/NTP Director Linda Birnbaum, Ph.D., on all management issues affecting the Institute, ranging from acquisitions, administrative services, and information services to financial management, facilities management, and the Institute's proactive environmental sustainability initiative.

In a message to employees, Birnbaum said, "I am pleased to announce that Ms. Joellen Austin will join the NIEHS family.… I also want to take this opportunity to thank [acting Deputy Associate Director for Management] Chris Long, who has enthusiastically and selflessly filled this very demanding role for the past 10 months [in an acting capacity]."

Austin comes to NIEHS from the National Institute of Neurological Disorders and Stroke (NINDS), where she had been associate director for management and executive officer since February 2007. After joining NINDS in 2000 as chief grants management officer, she served as deputy executive officer and acting executive officer there. Since joining NIH as a Presidential Management Fellow in 1989, Austin also served as chief grants management officer for the National Center for Research Resources and assistant grants policy officer in the NIH Office of Extramural Research.

Like many former Washington, D.C., and Bethesda, Md., federal employees, Austin is attracted by the quality of life in the Triangle and the unique mission of NIEHS. "I'm looking forward to joining NIEHS and doing my part to support our environmental health science mission," she said, "and I know I'll love working on such a beautiful campus every day." (Photo courtesy of Joellen Harper Austin)

Over the course of her career at NIH, Austin has been recognized as an outstanding administrator, manager, and supervisor. She has served on a number of high-profile NIH committees and is the current chair of the NIH administrative training committee, which oversees the NIH career development programs.

Austin received a Master of Science in management degree through the Sloan Master's Program at the Stanford Graduate School of Business in 2003. In addition, she holds a Master of Public Affairs from the Lyndon B. Johnson School of Public Affairs at the University of Texas at Austin, and a Bachelor of Arts in economics and government from Skidmore College.

Austin is a 2006 graduate of the U.S. Department of Health and Human Services Senior Executive Service (SES) Candidate Development Program, an intensive 18-month program of developmental experiences and formal training leading to SES certification by the U.S Office of Personnel Management. Austin was appointed to the SES in February 2007.

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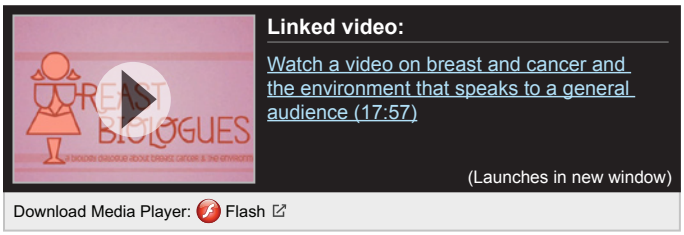
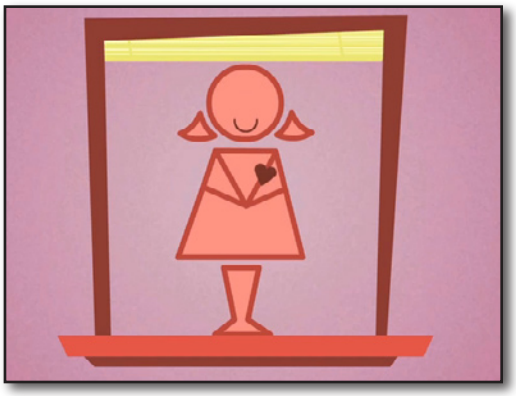
NIEHS grantee honored for new video on breast cancer research

By Ian Thomas

In recognition of its groundbreaking new video, "The Breast Biologues: A biology dialogue about breast cancer and the environment," the NIEHS-funded Bay Area Breast Cancer and the Environment Research Center (BABCERC) was recently presented with the esteemed "Award of Distinction." The video won over stiff competition from thousands of entries in the International Academy of the Visual Arts 2011 Communicator Awards competition.





The film uses this image of a young woman in the window of susceptibility during puberty, to help communicate the importance of timing of exposure in the development of breast cancer. (Image courtesy of Zero Breast Cancer)

The direct result of seven years of collaborative study by researchers Zena Werb, Ph.D., at the University of California San Francisco (UCSF), Paul Yaswen, Ph.D., at the Lawrence Berkeley National Laboratory, and Mary Helen Barcellos-Hoff, Ph.D., at New York University's Langone Medical Center. The video, animated by Lori Schkufza, is an engaging15-minute educational documentary that blends a scientific account of present day environmental breast cancer research with a timely, common-sense approach, making its message readily accessible to anyone from career researchers to the average high school freshman.

"Communicating basic science research is a challenge because of the complex concepts and technical language," said spokesperson Casandra Aldsworth, in a recent press release. Aldsworth serves as the community outreach and education coordinator at Zero Breast Cancer, a nonprofit organization and BABCERC's primary arm for community engagement. "In 'The Breast Biologues,' we tried to show the latest research about breast cancer and the environment in a way that many audiences could understand using animation and time-lapse microscope images."

The BABCERC, funded from 2003 to 2011, was based at UCSF and led by Robert Hiatt, M.D., Ph.D., currently the director of population sciences at the school's Helen Diller Comprehensive Cancer Center, BABCERC was one of four NIEHS-funded centers in the U.S. tasked with studying environmental causes of breast cancer by focusing on mammary gland development during puberty, a time when the breast may be particularly vulnerable to environmental influences. Falling under its research umbrella was a basic scientific study, an epidemiology study, and a community outreach and translation core.

In 2010, the Centers transitioned to the Breast Cancer and the Environment Research Program, a nationwide network of grants, jointly funded by NIEHS and the National Cancer Institute, that engages both laboratory and population-based research to study puberty and other windows of susceptibility, or specific time periods, when the developing breast may be more vulnerable to environmental exposures.

"As an organization, the video is helping us to achieve our goal of increasing awareness of the role of the environment in breast cancer prevention," Aldsworth explained. "We are honored that it has been recognized for its creative merits by the industry's best."

Hosted annually by the International Academy for the Visual Arts, the Communicator Awards honor outstanding achievement in the ever-evolving world of traditional and interactive media. Judged and overseen by the organization's more than 550 members, spanning a wide range of media disciplines, the annual competition draws the works of numerous industry giants, including Disney, HBO, and MTV. For the complete list of 2011 winners, visit the Academy's Web site at iavisarts.org.

To learn more about the Bay Area Breast Cancer and the Environment Research Center, or to view *The Breast Biologues* online, visit www.bayarea.bcerc.org. Official media kits containing both the video and accompanying comic book, offered in English and Spanish, are available upon request while supplies last.

(Ian Thomas is a public affairs specialist in the NIEHS Office of Communications and Public Liaison)

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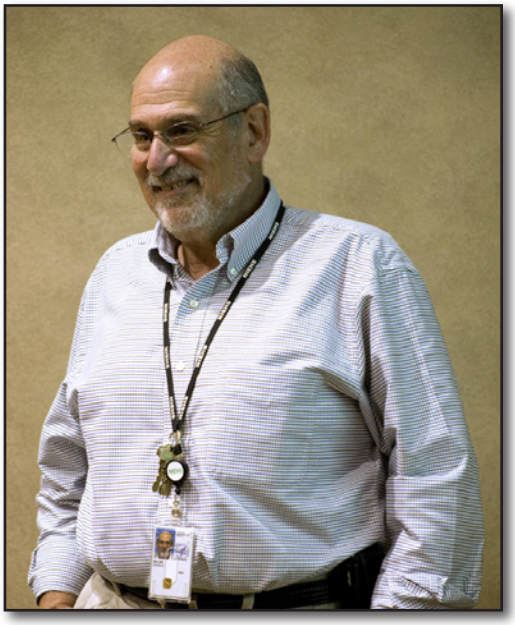
Miller welcomes and challenges 2011 summer interns

By Eddy Ball

Nearly every one of the 50 students participating in the 2011 NIEHS Summer Internship Program (SIP) attended a talk June 16 by Acting Scientific Director David Miller, Ph.D. Miller gave the interns a welcome and orientation to NIEHS, and he challenged his young audience to make the most of their summer experience at the Institute.



Miller told his audience, "It [research] is fun. If it wasn't fun, I wouldn't be doing it." (Photo courtesy of Jennifer Weinberg)

The program opened with remarks by SIP Coordinator Debbie Wilson and Deputy Scientific Director Bill Schrader, Ph.D., who talked about upcoming scientific talks and career development training for the interns. As they spoke, interns could see on the screen behind the speakers a photo of a much younger Miller, circa 1975, in a rustic lab in Maine.

The official title of Miller's presentation was "Welcome to NIEHS," but the talk was as much about Miller's own career path, his enthusiasm about scientific discovery, and how the different types of scientific research tie into one another at NIEHS.

A look back at seminal experience

As he talked about the experiences that shaped his journey through chemistry, biochemistry, and physiology, Miller's take-home message was simple and far more important than many of his listeners might realize until this summer is behind them. "Make the most of this opportunity to see what research is all about," Miller urged the interns, "because starting is very important."

Miller traced his own start in research to his experience in the summer of his sophomore year as part of the Undergraduate Research Participation Program at the University of Maine. "It was really a seminal event for me," Miller said about working in his chemistry professor's lab, "because it convinced me that what I wanted to do with my life was do scientific research."

"That experience was the most important experience I had in four years as an undergraduate," Miller continued, "because it basically showed me what I could do and what I was good at doing. You now have an opportunity for that experience, to ask and answer those questions… to have a chance to think about where you might end up and how to get there."

Miller's path to NIEHS and integrated environmental science

The internship in the professor's lab sparked interests in research that led Miller from chemistry into biology for a zigzag journey from bird studies on exposure to the pesticide DDT and eggshell thinning as a postdoc in Maine, to research into the blood-brain barrier and his current role as head of the NIEHS Division of Intramural Research.

When Miller turned to the structure of research at NIEHS, he discussed the organization, mission, and integration of research conducted within the Institute's many individual laboratories and groups. While the mission of NIEHS, Miller said, is better understanding the impact of environment on health, he also noted that a priority for senior scientists is creating the next generation of biomedical researchers. "And, that could include you," he told the interns.

Miller gave his audience an introduction into how basic research, toxicological research, clinical research, and epidemiological research feed into one another in a multi-directional interchange of communication. He illustrated this process with several examples, including global climate change, breast cancer research, and the large scale GuLF STUDY now underway to investigate the effects of the Gulf oil spill on cleanup workers. Miller tied "the really big question of how" into the overarching goal of NIEHS — preventing disease and maximizing public health — and told the interns, "This summer, you're a part of all this."

The Summer Intern Program

Along with their hands-on laboratory experiences, NIEHS offers summer interns a full program of training, career development, and scientific presentations, to complement their summer experience at the Institute.

As in past years, the high point of the program is the end-of-summer poster competition, where the interns will present the results of their work in the lab. Some of their projects will go on to become publications with the intern as first author and presentations at meetings of professional groups.

The interns will return to their high schools, colleges, and graduate programs in the fall better trained, more experienced, and, in some cases, transformed by the things they've done and the people they've met at NIEHS.

The meeting room where Miller spoke was barely sufficient to accommodate the turnout for his talk. (Photo courtesy of Jennifer Weinberg)

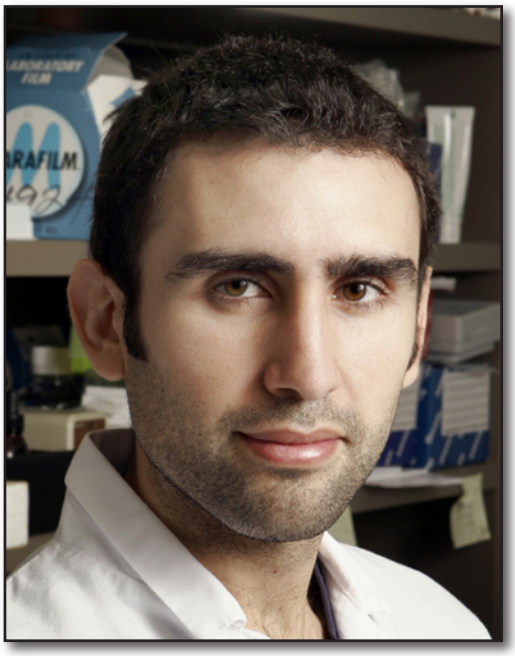
Intern Brian Rogers, a second year medical student, appeared engaged in his seat in the front row, as Miller talked about the importance of taking full advantage of the Institute's resources for a productive summer experience. (Photo courtesy of Jennifer Weinberg)

Like several of her peers, this intern appreciated the way Miller flavored his narrative with well-timed comic relief. (Photo courtesy of Jennifer Weinberg)

NIEHS fellow receives Endocrine Society Presidential Poster Award

By Ian Thomas

NIEHS visiting fellow Javier Revollo, Ph.D., received the Presidential Poster Award at ENDO Expo 2011: The 93d Annual Meeting of the Endocrine Society. Revollo's poster depicted his most recent research on glucocorticoids, steroid hormones that manage a variety of physiological processes, most notably metabolism and immunity.



Presidential Poster Award winner Revollo (Photo courtesy of Steve McCaw)

"This study was inspired by our need to better understand how glucocorticoids work," Revollo explained. "Initially, we hoped to simply define the role of Hes1 in glucocorticoid signaling, and I feel that we've certainly accomplished that and much more. Ultimately, we discovered that Hes1 is actually a major regulator of the signaling process."

Given the broad use of glucocorticoids in many of today's prescribed drugs, the possible applications of this particular study appear promising, an opinion shared by Revollo's postdoctoral advisor and the Chief of NIEHS' Laboratory of Signal Transduction, John Cidlowski, Ph.D.

"Through the course of his research, Javier has discovered a novel pathway that could eventually lead to new approaches in treating inflammatory disease in men," Cidlowski noted.

Hailing originally from La Paz, Bolivia, Revollo recalls how his interest in science began at an early age through a childhood fascination with the many exotic insects of the region. That interest later took him to the University of Wisconsin, where he studied genetics before eventually moving on to Washington University, St. Louis where he earned his Ph.D. in molecular cell biology while working extensively on the biochemistry of aging. Now, having settled comfortably into life as a resident of Research Triangle Park, Revollo says he enjoys his work with the Institute, as well as collaborations with his fellow scientists and peers, many of whom he credits for much of his success.

"It's always exciting to have one's hard work recognized, but I couldn't have accomplished this honor without the unwavering support of my mentor, Dr. Cidlowski, my fellow lab colleagues, and many other wonderful individuals here at NIEHS," Revollo said. "This award represents team effort and collaboration, and I am very grateful to everyone for that input."

Founded in 1916, The Endocrine Society is the world's oldest, largest, and most active international organization devoted to research on hormones and the clinical practice of endocrinology. This year's meeting was held in Boston, Mass. and attracted more than 7,800 scientific attendees and 2,600 abstract presentations from around the world.

(Ian Thomas is a writer/editor in the NIEHS Office of Communications and Public Liaison)

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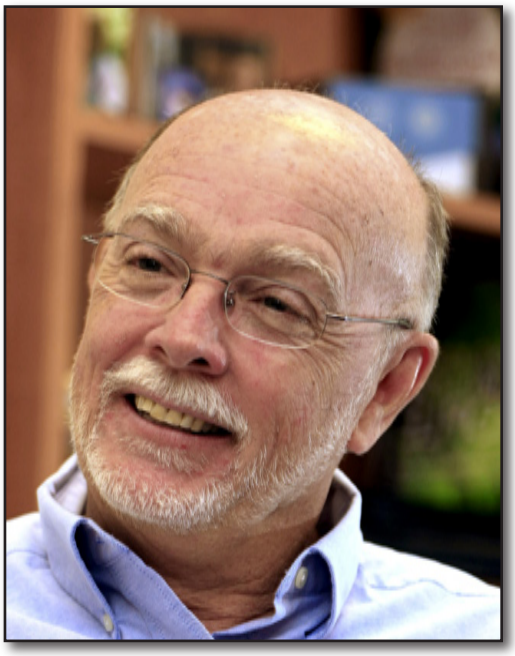
Suk honored by combustion emissions group

By Eddy Ball

NIEHS Superfund Research Program (SRP) founder and Director Bill Suk, Ph.D., was recognized by colleagues with the Adel Sarofim Award for Excellence in Combustion Research. Suk received the award at the 12th International Congress on Combustion By-Products and Their Health Effects: Combustion Engineering and Global Health in the 21st Century – Issues and Challenges, held June 5-8 at Zhejiang University in Hanzhou, China.



Along with leading the NIEHS SRP, Suk is the director of the NIEHS Center for Risk and Integrated Sciences. (Photo courtesy of Steve McCaw)

The award plaque praised Suk for "Outstanding Professional Achievement in Championing Research on the Origin, Fate, and Health Effects of Combustion Emissions." Suk said afterwards that he was honored by his colleagues' recognition, "But I feel the award really acknowledges the ongoing support for interdisciplinary research, linking applied combustion engineering with basic combustion engineering with health consequences, by the NIEHS Superfund Research Program over the past 20 plus years."

Balancing Suk's self-effacing assessment of the award was his colleague, Louisiana State University (LSU) chemist Barry Dellinger, Ph.D., chair of the congress' executive committee and an SRP grantee. "The award is well deserved," Dellinger said. "Bill pioneered much-needed support of interdisciplinary research that couples biomedical research with research in engineering and the physical sciences, something no one else was doing at the time. Bill's vision and leadership are what's made that happen."

The award is named for chemical engineer and combustion research pioneer Adel Sarofim, Sc.D., who is a senior technical advisor at Reaction Engineering International and former Presidential Professor in the College of Engineering at the University of Utah. Work by Sarofim spanning more than 50 years has led to important advances in combustion science and reductions in the release of pollutants from fossil fuel combustion.

Founded in 1990, the International Congress on Combustion By-Products and Their Health Effects meets biennially to share new developments in the field with scientists from around the world. Suk's award is the second one presented since it was first given in 2007 to Sarofim himself. In 2009, Dellinger was honored for his contributions to combustion engineering.

Along with major support from NIEHS and LSU, the congress enjoyed sponsorship by the National Science Foundation, Electric Power Research Institute, Navistar, Coalition for Responsible Waste Incineration, State Key Laboratory of Clean Energy Utilization at Zhejiang University, Institute for Thermal Power Engineering at Zhejiang University, and Ministry of Education of the People's Republic of China.

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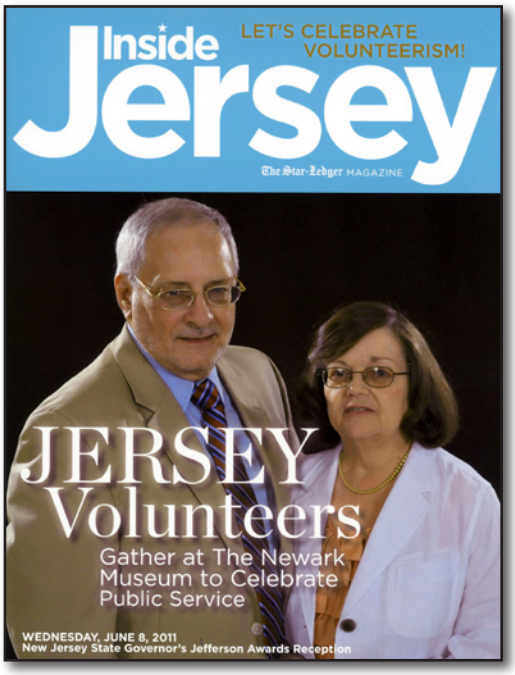
NIEHS partner honored for environmental stewardship

By Eddy Ball

NIEHS Public Interest Partners member Mary Lamielle was honored for her environmental stewardship June 8 in Newark, N.J., where she received the PSEG (Public Service Enterprise Group) Environmental Stewardship Governor's Jefferson Award.



The Star Ledger magazine "Inside Jersey" showcases Mary Lamielle, right, and husband Charles in its coverage of the Jefferson Award's ceremony. (Photo courtesy of the Star-Ledger)

Since 2007, the Jefferson Award program has recognized citizens who make extraordinary contributions to their communities and celebrated the power of volunteerism in New Jersey to improve the quality of life there. This year's awards honored 19 individuals, selected from more than 1,000 nominees.

A tireless advocate for people disabled by chemical sensitivities

Lamielle is the founder and executive director of the National Center for Environmental Health Strategies (NCEHS), Inc. in Voorhees, N.J. NCEHS is an organization that fosters the development of creative solutions to environmental health problems, pursuing a mission of protecting the public health, and improving the lives of people affected by chemical and environmental exposures. She was nominated for the Jefferson by Claudia Miller, M.D., who co-authored the landmark study of chemical sensitivity and intolerance for which the New Jersey Department of Health was awarded the World Health Organization's Macedo Award; Diane Reibel, Ph.D., a professor at the Jefferson Medical College; and Jane Nogaki, former vice chair of the New Jersey Environmental Federation.

In her letter of nomination, Reibel wrote, "For thirty years through her volunteer efforts, she [Lamielle] has been a passionate educator and advocate on behalf of people sick from chemical exposures and a protector of public health" — often, Reibel noted, as Lamielle struggled with her own illness caused by environmental exposures.

Reibel, who first met Lamielle 24 years ago, pointed to her friend and colleague's many pioneering accomplishments. These include initiating the landmark N.J. Study of Chemical Sensitivity; providing invited congressional testimony on the Indoor Air Quality Act; securing the first congressional funding for research on chemical sensitivities; serving on the expert panel convened to examine this issue; working to secure U.S. Department of Housing and Urban Development recognition of chemical sensitivities as a disability; and securing acknowledgement of chemical sensitivities as a disability in the Americans with Disabilities Act.

An honor recognized nationwide

The Jefferson Award program is administered by the N.J. Governor's Office of Volunteerism, the Star-Ledger newspaper, and the Community Foundation of New Jersey. PSEG, Verizon, PNC Bank, and Becton, Dickinson and Company (BD) are corporate underwriters of the awards. In addition to environmental stewardship, the program recognizes individuals, businesses, and groups involved in activities ranging from arts and education to health care and community services.

Lamielle was one of four New Jersey nominees invited to the Jefferson Awards ceremony in Washington, D.C., June 20-22. Highlights included a visit with one of their state's senators, a visit to the White House, and two evening events, one of which was the black tie Jefferson Awards for Public Service emceed by Kathleen Kennedy Townsend, daughter of Senator Robert Kennedy and niece of award cofounder Jacqueline Kennedy Onassis. National honorees this year include Supreme Court Justice Ruth Bader Ginsburg.

Lamielle is one of the 25-member Public Interest Partners, which is made up of representatives of diverse groups, including disease, disability and environmental education, and advocacy organizations. Members offer NIEHS community perspectives on the research agenda of NIEHS, and serve as a key contributor to the translation of research findings for the public, policy makers, and private foundations. Lamielle has been invited to participate in the 2011 NIEHS Strategic Planning Stakeholder Community Workshop July 12-14 in Research Triangle Park, N.C.

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Lamielle calls for more answers

"I hope that the Jefferson Award for Public Service will heighten visibility of what has, for decades, been an invisible public health problem," Lamielle said, following the award ceremony. "Eighteen years ago, members of an expert panel on chemical sensitivities and intolerances, convened by the Agency for Toxic Substances and Disease Registry, with directed congressional funds, recommended forming an interagency committee across [or which would consist of representatives of] disability, regulatory and research agencies, and clinical research using an environmental medical unit. Our organization continues to call for an interagency committee to catalyze a federal agency response to address these disabilities."

"The recently released Action Agenda for the Centers for Disease Control and Prevention National Conversation on Public Health and Chemical Exposures [see related story] recommends research on chemical sensitivities and intolerances using an environmental medical unit. Nearly two decades have passed. Millions more Americans report serious illness and disability due to chemical exposures," Lamielle continued. "It's time to act."

Klotz departs NIEHS for position at Sanford-Burnham

By Archana Dhasarathy

NIEHS training mainstay Diane Klotz, Ph.D., left the Institute in June for a position at the Sanford-Burnham Medical Research Institute in San Diego. Klotz has served as director of the NIEHS Office of Fellows' Career Development (OFCD) part time starting in May 2007, transitioning into full-time director in September 2007.

In her new job at Sanford-Burnham, a National Cancer Institute-funded cancer center, Klotz will oversee both the graduate and programming training policies. She will also be responsible for oversight of the graduate and summer programs, as well as training policy development and implementation at both the La Jolla, Calif. and Lake Nona, Fla. locations of Sanford-Burnham.

The driving force behind the OFCD

Following in the footsteps of her predecessor, Debbie Swope, Ph.D., Klotz continued to foster an excellent training environment for postdoctoral fellows at NIEHS. A strong advocate for the fellows, Klotz helped ensure that they were exposed to a wide variety of training and networking opportunities.

"During her time at NIEHS, Diane has helped countless trainees successfully navigate the complexities of research, administration, and interpersonal relationships," said Erin Hopper, Ph.D., a trainee in the Mass Spectrometry Group. "She cared immensely for the fellows' career development and always strived to bring the best possible resources to fellows interested in a wide spectrum of career opportunities," agreed Raj Gosavi, Ph.D., a fellow in Structure and Function Research Group.

NTA Steering Committee Co-chair Nisha Cavanaugh, Ph.D., an IRTA fellow in the NIEHS DNA Repair and Nucleic Acid Enzymology Group said about her experience with Klotz, "She has been a great mentor and advisor for me. As co-chair of the NTA Steering Committee, I have worked closely with her and she has always provided guidance and support with every concern that the committee has raised."

Klotz also worked tirelessly and patiently to help international fellows handle a range of issues. "Many international fellows were hesitant to meet with her because they thought their English skills were poor," said Sung-Yong Hwang, Ph.D., a visiting fellow in the Calcium Regulation Group. "However, Diane Klotz was always very patient and professional. I met with her many times, and she always encouraged me and gave me practical assistance with my resume and other things," Hwang added.

In fact, Klotz has been responsible for many postdoctoral fellows transitioning to successful careers away from the bench. "Diane Klotz was an incredibly valuable resource at NIEHS when I applied for my current job at [the law firm] Alston and Bird," said former NIEHS postdoctoral fellow, Jeffrey Sunman, Ph.D. "I will always be grateful for both the help and the enthusiasm that she brought to each of our meetings," he added.

Like her predecessor, Klotz brought to her job her own experiences as a postdoc, negotiating the twists and turns of career development. During her four years as OFCD director, Klotz expanded the training program at NIEHS and earned a place in the hearts of the many trainees whose lives she touched. (Photo courtesy of Steve McCaw)

In his announcement to trainees, NIEHS Deputy Scientific Director Bill Schrader, Ph.D., described Klotz as "a mainstay of training at NIEHS," and noted, "To say she'll be missed and hard to replace is an understatement." Schrader congratulated her on this advancement in her career. (Photo courtesy of Steve McCaw)

The importance of networking

In addition to her primary position as director of the OFCD, Klotz also served on several institute-wide training committees, including the NIH Training Director's Committee, and was the chair of the Board of Directors for the National Postdoctoral Association (NPA), where she now sits on the Advisory Council. "Diane Klotz's commitment to improving the postdoctoral experience, both at NIEHS and on a national level, is what makes her such a treasure," said Lori Conlan, Ph.D., director of the NIH Office of Intramural Training and Education.

Klotz strongly advocated networking as a key to finding the right job after completing postdoctoral studies. "Good science is of course a priority, but building and maintaining a professional network is equally important in today's extremely competitive market,"

she said. Indeed, it was her networking skills that helped land her current position. Klotz was recruited by the vice president of human resources at Sanford-Burnham — someone whom she had previously served with on the NPA board of directors.

Everyone who worked with Klotz at NIEHS wishes her all the best in this important next step in her career.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

Roots in the postdoctoral experience: A multi-faceted career at NIEHS

Klotz' first experience at NIEHS was as an Intramural Research Training Award (IRTA) fellow with former NIEHS scientist Richard DiAugustine, Ph.D., in the Laboratory of Molecular Carcinogenesis. "Diane's most notable research effort while in the Hormones and Cancer Group was a study that examined a variety of synthetic and environmental estrogens," said DiAugustine, who retired a few years ago from NIEHS. "This was one of the first studies to show that environmental estrogens mimic estradiol in vivo, by stimulating a growth factor pathway," he added. She stayed on as a research fellow to actively pursue her work, including some collaborative projects with Ken Korach, Ph.D., principal investigator and chief of the Laboratory of Reproductive and Developmental Toxicology.

During her postdoctoral career, Klotz was also actively involved in National Trainees Assembly (NTA) and the National Postdoctoral Association (NPA). She served as chair of the NTA Steering Committee for a year and a half, on the NPA board of directors for two years, and as chair of the NPA for a year.

These experiences increased her interest in how a scientific organization functioned, and helped her transition to becoming director of the OFCD. "Rather than focus on just my own research, I became more interested in helping to develop a flourishing research organization as a whole," said Klotz. "I felt lucky working at NIEHS, because I was not completely isolated from science. I could still go to scientific seminars and speak with people about their research," she added.

When asked what she would miss the most at her new job, Klotz replied, "The people I've worked with, and the friendships I've built, both personal and professional."

She added, "I will also miss all of the fellows I have worked with. But there are many great mentors at NIEHS and I am especially encouraged by the level of engagement by our tenure track PIs, and I look forward to hearing of much continued success for all the NIEHS postdoctoral fellows."

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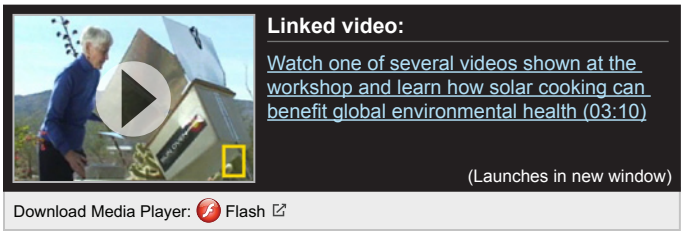
Local students energized by climate change workshop

By Ed Kang

From June 13 – 17, 26 academically talented juniors and seniors, representing nearly every high school in Durham County, made the daily trek to Research Triangle Park to take part in hands-on activities, experiments, demonstrations, and spirited debates at a High School Student Workshop on Climate Change.

Conducted by scientists from NIEHS and the U.S. Environmental Protection Agency, the workshop was the first of its kind to educate students about the relationship between climate and health. The five-day program featured more than 30 sessions related to environmentalism, health, ecology, sustainability, and communication.



Durham County high school students learned that sustainability and sacrifice are not necessarily correlated. Here, Shar Samy, Ph.D., center, a postdoc at EPA, uses a solar cook stove to deliver a fresh batch of chocolate chip cookies. (Photo courtesy Ian Boudreau and EPA)

"I enjoyed the workshop for all the different perspectives," said Jayati Vyas, a 16-year-old rising junior at the Durham School of the Arts. She was one of 17 young women accepted to participate in the workshop. Vyas' perspective on climate change was transformed by her participation in the workshop — a phenomenon shared by many in the group. "Just because we're in the U.S. doesn't mean we can escape the effects of climate change," she learned.

Filling a gap in environmental education

Bono Sen, Ph.D., science education and outreach manager for NIEHS' journal Environmental Health Perspectives, had the idea for a unique program focusing on the health impacts of climate change for more than a year. The inspiration for the week-long event came from a local student workshop on climate change held last year at the University of North Carolina.

"But a missing piece was nagging at me," Sen explained.

That piece was the toll of climate change on human health. "So the goal of this workshop was to build climate literacy – to help connect the dots between climate change and human health."

Students learned to model real-world scenarios. In this exercise, Anthony Fantasia of Riverside High School, center, and Johnnie Tabron, Jr., of the Southern School of Engineering, use everyday fluids to better understand how diseases are transmitted by mosquitoes. As a consequence of climate change, the mosquitoes are changing their range, lifespan, and reproductive cycle. (Photo courtesy Ian Boudreau and EPA)

Sen's vision became a major theme for the NIEHS/EPA event. "This is a new way of thinking," commented Sen on the current discourse surrounding climate change. "I am very happy to see the students incorporating human health into their perspectives on climate change."

Sen collaborated with Kelly Leovic, director of EPA-RTP Environmental and STEM (science, technology, engineering, and mathematics) Outreach, and Carly Carroll, science education program coordinator for EHP, to help draw from the collective knowledge base and strengths of both NIEHS and EPA.

John Balbus, M.D., senior advisor for public health at NIEHS, was one of the many enthusiastic speakers recruited. He told the students, "Maybe it's not global warming, but it's definitely global weirding, and this extreme weather can have all sorts of cascading effects on health." He challenged students to make a difference. "Have courage to live consciously — do the little things. They are an expression of your commitment."

Public policy and risk communications were also part of the week's agenda. Cody Leovic of Northern High School, and Kelsey Bennett of Jordan High School, engage their classmates in a discussion of the costs verses benefits of electric car use. (Photo courtesy Ian Boudreau and EPA)

That commitment is not just a feel-good slogan, it's a fundamental principle built into the students' program from the beginning. "The unique part about the workshop is the grass-roots aspect," remarked Sen. "This is not about polar bears or Africa, but about the health and environment of people in the local area."

Carroll, who managed the organization and logistics for the program, will be keeping tabs on the students as they return to their academic homes. "One of the requirements for the program is that these 26 students do an extension project, where they go back to the classroom and become a proactive agent for change."

Carroll, left, and Sen called upon the rich resources of EHP news features and scientific studies and the volunteers from NIEHS and EPA as they collaborated with Leovic to design the workshop. (Photo courtesy of Steve McCaw)

Blogs, videos, in-class presentations, and starting up new clubs are among the ideas already proposed by the participants. "These students are now experts for their classmates," Carroll said proudly of her new protégés.

Vyas, who aspires to pursue a career in medicine and volunteers at Duke Hospital, is anxious to recommend the workshop to her classmates and share some of the concepts she learned during the week. "Climate change is scary, but if I can make a small difference with the 500 kids at my school, maybe I can start a domino effect."

Leovic and Sen agreed that the EPA and NIEHS partnership benefitted the students by offering dual perspectives on the same problem. Sen reflected on the week by saying, "I think we can say that we have created our first cohort of climate ambassadors."

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

An enlightening experience for students — and their teachers

For most high school students, June kicks off a much-needed vacation from the rigors of school. For others it means taking on a summer job to pay for upcoming college expenses. But for a few dozen Durham County, N.C. students, it meant spending an exciting week learning about the science behind climate change and related health effects. For the volunteers who gave presentations at the workshop, it was an opportunity to experience cross-disciplinary collaboration.

Designed as part of the EHP Science Education Outreach Program, the workshop drew on the talents of specialists from both NIEHS and EPA. NIEHS speakers and their topics at the High School Student Workshop on Climate Change included:

- Human Health Systems - Huei-Chen Lao
- Climate Change and Human Health - John Balbus, M.D.
- Vector-borne Diseases - Lihn Pham, Ph.D.
- Communicating Climate Change - Kimberly Thigpen-Tart, J.D.
- Surviving Climate Change: a Team-building Exercise - Ed Kang
- The Futures' Wheel - Valerie Davis, Ph.D.
- Career Panel - Michael Humble, Ph.D., Quiana Childress, Amber Haynes, Darshini Trivedi, Ph.D.
- Debating the Kyoto Protocol - Erin Hopper, Ph.D.

The efforts of these NIEHS presenters were clearly appreciated. As one student, Anthony Fantasia of Riverside High School, explained, he came into the activity thinking it would focus on "what to think about climate change." He soon realized that the mission of the activity was to provide the science to help students understand the facts and reach their own conclusions. "One of the things I enjoyed most about the workshop was all the science," he remarked.

Throughout their week in the workshop, the students were exposed to concepts the public doesn't hear about every day —— from paleoclimatology, adaptation strategies, and mitigation techniques, to the latest technologies in solar panels and cook stoves. For their part, some of the veteran presenters found themselves learning from the expertise of their fellow speakers.

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NIEHS recognized for composting

NIEHS scored an organization honorable mention in the Environmental Stewardship category of the FY2010 U.S. Department of Health and Human Services (HHS) Green Champions Awards Program.

The program singled out NIEHS for composting achievements that diverted 15,790 lbs. of pre- and post-consumer cafeteria waste from the landfill, while reducing greenhouse gases, such as methane and carbon dioxide, normally produced during waste decomposition. In FY2010, over 95 percent of the Institute's total cafeteria waste was either composted or recycled, surpassing the NIEHS 2010 Environmental Management System goal of 10,000 pounds.

In her announcement of the results of this year's competition, NIEHS Sustainability Coordinator Trisha Castranio acknowledged the collective contributions of people at NIEHS toward recognition of the Institute's program. Last year, NIEHS won the FY2009 Organization Green Champion Award (see story).

"We are proud of the example we set as an environmental institute to protect human health and the environment in our work as well as in our daily life," Castranio wrote to her colleagues. "Your effort embraces the spirit of our sustainability program and commitment to reducing our environmental footprint."

Compost from the offsite facility is returned to the NIEHS campus for use as mulch around landscaped trees and in the shrubbery beds reducing the need to purchase these items. "These actions support a healthy environment in our Institute while demonstrating good environmental stewardship and sustainable practices to our community," Castranio said.

This year marks the third annual HHS Green Champions Awards, which honor outstanding HHS employees and Native American tribal members involved in various sustainability projects in the areas of electronic stewardship, energy and water conservation, environmental management, green procurement, sustainable buildings, and transportation and fleet management.

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Henry organizes session for "Sustainable Remediation 2011"

By Eddy Ball

NIEHS Health Scientist Administrator Heather Henry, Ph.D., organized a multi-agency session on "Human Health" for the "Sustainable Remediation 2011: State of the Practice - Green Chemistry, Human Health, and Environmental Response" meeting June 1-3, 2011 at the University of Massachusetts-Amherst (UMass-Amherst).

Henry is a part of the NIEHS Superfund Research Program, which was co-sponsor of the Sustainable Remediation meeting organized by the U.S. Environmental Protection Agency (EPA) Office of Superfund Remediation and Technology Innovation.

Henry and Marjorie Aelion, Ph.D., dean the UMass-Amherst School of Public Health and Health Sciences Administration, moderated the June 2 session. They and their colleagues strove to raise awareness of potential health risks from products and practices that may be environmentally friendly, but still may pose a possible threat to people.

Keynote speaker Chris Portier, Ph.D., director of the Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry (ATSDR), discussed the human health implications of reuse and redevelopment of former brownfields and industrial buildings. He identified a number of sites where ATSDR conducted investigations of human exposure to various hazardous substances because the previous use of a site was not fully investigated or mitigated.

The breakout sessions on Human Health featured new guidelines for school and daycare siting to prevent exposures when industrial sites are acquired for reuse. In addition, there was a concern about the use of spray foam insulation — a "green" product because of its energy efficiency benefits — and its potential impact on children's health.

Abstracts and presenter biographies are available online.

The co-organizers and speakers for the Human Health Session gathered following their presentations. Standing in the front row, left to right, are Henry; Sharee Major Rusnak, Connecticut Department Health; Marybeth Smuts, Ph.D., EPA; Tarah Somers, ATSDR; Aelion; Gary Perlman, ATSDR. Shown on the back row, left to right, are Lee Newman, Ph.D., State University of New York College of Environmental Science and Forestry; Meg Harvey, Connecticut Department of Public Health; Deborah Burgin, Ph.D., ATSDR; Ryan Costello, ATSDR; and Portier. (Photo courtesy of Richard B. Newton)

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Science Notebook

Duke researcher gives 2011 Rodbell Lecture

By Robin Arnette

Every breath that a terrestrial organism takes is critical to its survival, but the lung is often overlooked in terms of its importance. One researcher, however, who finds beauty in the organ, is Brigid Hogan, Ph.D. Hogan studies lung development in embryonic mice, and hopes her work will lead to a better understanding of birth defects and possibly how environmental factors influence the process of lung development. She discussed her research on June 14 at NIEHS as the 2011 Dr. Martin Rodbell Lecture Series speaker.

Hogan is the George Barth Geller Professor and chair of the Department of Cell Biology at Duke University Medical Center. She also serves as director of the Duke Stem Cell and Regenerative Medicine Program. (Photo courtesy of Jennifer Weinberg)

Hogan began her talk by describing the lung as a highly vascularized, branched system of airways. The tree-like organization gets smaller and smaller, ending at the periphery with tiny air sacks called alveoli. She said a layer of epithelial cells line the alveoli, and part of the intricacy of the lung hinges on the many different cell types that line the airway (see text box). She wondered, though, about how did all of these cell types begin. How were they generated, and how were they able to organize properly? These questions formed the basis of her research.

"We determined that in a nine-day old mouse embryo, the lung starts as two little buds which come off on the ventral part of the foregut," Hogan explained. "Thanks to the research contribution of several labs, we now know that signaling pathways in the mesoderm and endoderm drive the expression of the transcription factor Nkx2-1 at the tip of the ventral foregut where the buds form."

The role of signaling pathways in lung development

To determine whether the epithelia cells in the tips of the foregut were able to develop into many different types of cells, one of Hogan's postdocs tracked the cells' descendants. The experiment, called lineage tracing, occurred over a period of several days, and began by marking individual tip cells using a pulse of tamoxifen, a drug that interferes with the activity of estrogen and is used to treat some types of breast cancer. Developmental biologists have co-opted it to switch on special "reporter" genes that can trace all the descendants of a cell in an organ as it develops.

Lecture host Williams shares interests with Hogan in the area of reproductive biology. (Photo courtesy of Jennifer Weinberg)

The lineage tracing results showed that the transcription factor Id2 (inhibitor of differentiation) is expressed specifically in these tip cells along with another transcription factor called Sox9. Id2 continues to be expressed in these cells until just before the structure gives rise to the alveoli. These findings have significant human health implications, because premature babies are born at a stage before alveolar cells are generated. Scientists need to know what controls this switch for making the terminal buds and how it can be protected in these babies.

Stem cells in the adult lung

After looking at embryonic tissue, Hogan asked if any of these multipotent cells remained in the adult lung. Another member of her team did a lineage tracing of secretory cells and found that even though they have differentiated characteristics, they could self-renew over a long period of time and help repair small airways after injury. Work with undifferentiated basal cells taken from other parts of the mouse lung demonstrated that these cells function as multipotent stem cells. Basal cells are found throughout the airways of the human lung, and as long-term stem cells, they may be vulnerable to changes induced by toxic and inflammatory agents.

Carmen Williams, M.D., Ph.D., an NIEHS researcher with dual appointments in the Laboratory of Reproductive and Developmental Toxicology and the Clinical Research Program, hosted the lecture and spoke afterward about the significance of Hogan's body of work. "Dr. Hogan's use of powerful mouse genetics techniques to perform lineage tracing experiments has enabled her to identify multipotent lung progenitor cells that could lead to new treatment modalities for human lung injury."

Fellow stem cell expert, Guang Hu, Ph.D., head of the NIEHS Stem Cell Biology Group, also attended the lecture and said, "Her studies help us better understand the lung's response to environmental toxins and have accelerated the development of stem cell-based therapies for lung diseases."

NTP postdoctoral fellow Erik Tokar, Ph.D., is a member of the NTP Inorganic Carcinogenesis Branch. (Photo courtesy of Jennifer Weinberg)

NIEHS/NTP Director Linda Birnbaum, Ph.D., left, presented Hogan with a statuette of Rodbell's hand as Deputy Director Rick Woychik, Ph.D., looks on. Hogan's souvenir is one of only 13 Rodbells presented since the series began in 1998, with an address by Nobel Laureate Martin Rodbell Ph.D., just weeks before his death. (Photo courtesy of Jennifer Weinberg)

Principal Investigator Anton Jetten, Ph.D., head of the NIEHS Cell Biology Group, seemed to find the talk specially thought provoking. (Photo courtesy of Jennifer Weinberg)

After the talk, Hogan, right, and Williams, left, participated in yet another Rodbell Lecture tradition. She joined Rodbell's widow, Barbara, in front of the main NIEHS building for a photo opportunity. (Photo courtesy of Jennifer Weinberg)

Epithelial cell types in the mouse lung

Trachea and the main stem of bronchi: ciliated, secretory, and basal cells

Bronchioli: ciliated, secretory, and neuroendocrine, but no basal cells

Alveolus: Type 1 and Type 2 cells

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Steady progress reported at SACATM

By Ernie Hood

The Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) meets only once a year, but with considerable progress during the past year in efforts to reduce, refine, or replace animal use in chemical and product safety testing, there was much to discuss and digest at this year's SACATM meeting June 16-17 in Arlington, Va.

In its advisory role to the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), SACATM provides advice on priorities and activities related to the development, validation, scientific review, regulatory acceptance, implementation, and national and international harmonization of new, revised, and alternative toxicological test methods.

Stokes, flanked by NTP Associate Director John Bucher, Ph.D., left, and Niemi, right, discussed the impact of newly developed alternative testing methods of regulatory agencies safety testing. (Photo courtesy of Ernie Branson and NIH)

NIEHS/NTP Director Linda Birnbaum, Ph.D., in her welcoming remarks to the SACATM members; ICCVAM members, representing the 15 participating Federal agencies; and NICEATM staff in attendance, noted the organizations' successes. "ICCVAM and NICEATM continue to provide an effective process for achieving the regulatory acceptance of new safety testing methods," she said.

"The center and the committee have now contributed to the endorsement or adoption of 42 new alternative methods. 28 of these are *in vitro*, and over half of those *in vitro* methods involve human cells," Birnbaum explained. "Thanks to ICCVAM's continued, focused efforts, there are now approved alternatives for many different types of testing, including five of the six most commonly conducted safety tests." Nine of the 42 new alternative methods were put forward in just the past year, she noted.

Birnbaum, at microphone, expressed her appreciation for SACATM's steady progress in developing testing to reduce, refine, or replace animal use in chemical and product safety testing. (Photo courtesy of Ernie Branson and NIH)

Two new nominations to NICEATM and ICCVAM, both of which were unanimously supported by the committee, were also prominent in SACATM's agenda. The first, an *in vitro* pyrogen test method for assessing non-endotoxin pyrogens, is an extension of an existing method to screen for substances that induce fever, which is currently used only to detect gram-negative endotoxin. Validation and adoption of the *in vitro* method for non-endotoxin pyrogens would further reduce the use of rabbits, the current model for detecting fever reactions in various drugs and products prior to their commercial release.

The second nomination involves three types of *in vitro* diagnostic and potency assays for botulinum neurotoxins (BoNTs). The new tests are proposed to detect BoNT in suspected botulism poisonings in people and wildlife, and for testing therapeutic and cosmetic BoNT products, which were used in an estimated five million off-label cosmetic treatments in the U.S. in 2008. Rear Adm. William Stokes, D.V.M., director of NICEATM and executive director of ICCVAM noted, "these methods have the potential for more rapid and accurate public health and product testing, and could significantly reduce the number of mice used for BoNT testing throughout the world."

During a break in the proceedings, Stokes, left, joined KoCVAM Vice Director Soojung Sohn, center, and NTP Toxicology Branch Group Leader Rajendra Chhabra, Ph.D. (Photo courtesy of Ernie Branson and NIH)

SACATM chair Steven Niemi, D.V.M., from Massachusetts General Hospital, said it was very appropriate for the nominations to be front and center for the committee's business at the meeting. "They were both obviously very high priority, and will have a big impact on animal welfare as soon as they're adopted."

Meeting participants were also updated by representatives of ICCVAM's international partners. In-person presentations were made by collaborators from the Korean Center for the Validation of Alternative Methods (KoCVAM) and the Japanese Center for the Validation of Alternative Methods, and the panel was briefed by telephone by officials from Health Canada and the European Centre for the Validation of Alternative Methods, both of whom had taken in the meeting's proceedings by webcast.

Stokes praised the international cooperation ICCVAM and NICEATM have received. "It allows us to leverage resources, so we can share the cost and time that it takes to carry out expensive validation studies, and we can also work together so that we're more likely to be in agreement and can achieve faster acceptance of those methods internationally," he said.

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

SACATM participants gathered to celebrate the increasing acceptance of alternative testing methods. Standing, left to right, are Joy Cavagnaro, Ph.D., Access BIO, L.C.; Steven Hansen, D.V.M., American Society for the Prevention of Cruelty to Animals; Michael Olson, Ph.D., GlaxoSmithKline; Eugene Elmore, Ph.D., University of California Irvine; George Corcoran, Ph.D., Wayne State University; Sharon Meyer, Ph.D., The University of Louisiana at Monroe; Gary Wnorowski, Eurofins/Product Safety Laboratories; Linda Toth, D.V.M., Ph.D., Southern Illinois University School of Medicine; Daniel Wilson, Ph.D., The Dow Chemical Company; and Lori White, Ph.D., NTP. Sitting, left to right, are Birnbaum; Bucher; Stokes; Niemi; ICCVAM Chair Jodie Kulpa-Eddy, D.V.M., U.S. Department of Agriculture; Gwendolyn McCormick, D.V.M., Boehringer Ingelheim Pharmaceuticals, Inc.; and Karen Brown, Ph.D., Pair O'Docs Enterprises. (Photo courtesy of Ernie Branson and NIH)

Putting alternative test methods into practice

During the meeting, Stokes updated SACATM members on the groups' recent activities and priorities, as well as what he said was "a lot of progress" in domestic and international regulatory acceptance and adoption of ICCVAM-recommended alternative test methods. Among the past year's significant activities were:

- An international workshop on the state of the science and future directions in vaccine potency and safety testing, where there is enormous potential for reducing, refining or replacing the use of animals
- Two workshops on best practices for regulatory safety testing, covering ocular safety testing and allergic contact dermatitis hazard testing
- An ICCVAM Peer Review Panel meeting to evaluate an *in vitro* endocrine disruptor screening method, the LUMI-CELL ER® (BG1Luc ER TA) test method to identify substances with estrogen agonist and/or antagonist activity

Regarding the endocrine disruptor screening test, Stokes said that "it looks like a very promising method, and recommendations will be forwarded to both the U.S. agencies and to the international agency, OECD [Organisation for Economic Co-operation and Development], in the near future."

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T cells take center stage at NIEHS symposium

By Ernie Hood

NIEHS played host to a diverse group of some 100 scientists from the field of immunology June 9, with a daylong workshop titled "Emerging Concepts in T Cell Activation and Disease." The symposium, which was attended by more than 100 researchers, was organized by Donald Cook, Ph.D., principal investigator and head of the NIEHS Immunogenetics Group within the Laboratory of Respiratory Biology.

Cook, who organized the meeting, welcomed attendees to the symposium and presented his group's work on the immunology of allergic

Cook said of keynote speakers Trinchieri, above, and Paul, "It was an honor to have immunologists of their stature at the meeting. In addition to their outstanding presentations, they asked questions of the other speakers and interacted well with the meeting attendees." (Photo courtesy of Steve McCaw)

Public health and treatment implications

The meeting was an opportunity for scientists in the Research Triangle, N.C. area to hear from both local and international experts in the field and learn more about the mechanisms of T cell activation, the workhorses of the adaptive immune system. Under normal circumstances they help ward off infections, but all too often the delicately balanced immune system runs awry.

T cells are a component in almost all diseases, and have a substantial role in causing the pathology seen in many major chronic conditions, such as allergic asthma, diabetes, and arthritis. Modulating T cell response is an area rich in therapeutic potential, but, as Cook said, "To be able to do that effectively, it's going to be important to learn more about how T cells are activated, so that we can either raise the responses or lower them, depending on what we need to do for particular diseases."

The meeting also served to promote collaboration among T cell biologists in the Triangle area, by allowing local investigators with common interests to interact and learn more about each other's work. To that end, several scientists from Duke University and the University of North Carolina made presentations about their research programs and results. [see text box]

Showcasing authorities in T cell research

The symposium also attracted two of the leading lights of the field — Giorgio Trinchieri, M.D., chief of the Laboratory of Experimental Immunology within the Center for Cancer Research at the National Cancer Institute, and William Paul, M.D., chief of the Laboratory of Immunology at the National Institute of Allergy and Infectious Diseases. Both spoke about investigations into T cell activation and disease.

Trinchieri's research focuses on the interplay between inflammation and innate resistance and adaptive immunity, and the role of pro-inflammatory cytokines in the regulation of hematopoiesis, innate resistance, and immunity. He discovered interleukin-12

while at the Wistar Institute in 1989 and, for many years, has been characterizing the molecular mechanisms of interleukin-12 production and its role in tumor immunity, infections, and autoimmunity.

Paul's talk described the emerging knowledge about the fates and functions of CD4 T helper (Th) cells and the various cytokines produced by some of the major Th cell sub-types, particularly many forms of interleukins. Depending on the stimulus involved, such as a specific antigen, so-called naïve T cells differentiate into many subtypes through highly complex signaling processes. They perform a variety of functions in the immune response, and it is now emerging that they exhibit plasticity as well, further complicating an already complex picture.

Paul gave his talk an amusing and evocative title, "Cytokines and CD4 T cells: Dance partners at the immunology ball." His work with Interleukin 1 may lead to new strategies to prevent and treat viral and bacterial infections, especially through the development of next-generation vaccines to manipulate immune response. (Photo courtesy of William Paul)

T cell studies at NIEHS

Cook also had the opportunity to describe his group's work on the immunology of allergic asthma, which has identified a specific cell type, called a CD103+ dendritic cell, required for the initiation of allergic responses to inhaled allergens. The dendritic cell acquires inhaled allergens in the lung and presents them to naïve T cells in a way that promotes Th2 responses that are typically associated with allergic diseases. Therapies that inhibit CD103+ dendritic cell function could eventually be used to prevent or treat allergic asthma, Cook explained.

A common theme in the presentations was the growing awareness that immune responses are both more complex and more flexible than previously thought. As Cook explained, "Many molecules that have been traditionally thought to function in restricted T cell subsets actually function in multiple subsets of T cells and modulate the behavior of those subsets in unexpected ways. For example, specific transcription factors, which control the expression of genes, are involved in more types of responses than has been appreciated until now."

(Ernie Hood is a contract writer with the NIEHS Office of Communications and Public Liaison.)

Gunn was the only NIEHS grantee speaking at the symposium. With his counter-terrorism funding, he studies the prevention of inflammatory lung injury after chlorine exposure. (Photo courtesy of Steve McCaw)

Suited to a T

Each of the speakers at the T cell activation symposium presented new, exciting work in the field.

- **Michael Dee Gunn, M.D.**, Duke University, CCR-2-dependent and CCR-7-dependent DC populations differentially regulate T cell immune response: Gunn described studies of inflammatory cell migration within various forms of immune response. It appears that tissues imprint local dendritic cells to mount a characteristic immune response for that tissue, while cases of severe insult stimulate recruitment of CCR2-dependent monocyte-derived dendritic cells, in a robust Th1 immune response.

- **Roland Tisch, Ph.D.**, University of North Carolina, T cell co-receptor blockade and the re-establishment of self tolerance: Tisch has found that blockade of molecules on T cells known as CD4 and CD8 induces rapid reversal of diabetes in mice without affecting their immune responses to foreign antigens. The success of this approach suggests it might be effective for the treatment of other T cell-mediated autoimmune diseases such as multiple sclerosis and rheumatoid arthritis.

- **Mari Shinohara, Ph.D.**, Duke University, Novel intracellular isoform of osteopontin (iOPN) in antigen-presenting cells: Although the secreted form of the molecule osteopontin (OPN) is known to promote inflammation and immunity against microbial infections, Shinohara has found that intracellular OPN (iOPN) controls excessive TNF production by macrophages through simultaneous stimulation of CD40 and strong PRR signaling pathways. Her study has elucidated how OPN switches its pro-inflammatory role to an anti-inflammatory in the presence of adaptive immune cells that supply CD40L under acute infections.

- **Qi-Jing Li, Ph.D.**, Duke University, Harnessing microRNAs to micromanage T cell immunity: Li described his group's work on characterizing the role of non-coding RNAs (ncRNAs), specifically microRNAs (miRNAs), a novel class of small ncRNAs that mediate post-transcriptional gene silencing, in immune response. He focused particularly on the role of a specific cluster of miRNAs, miR-17-92, which among other functions comprehensively supports the CD4 T cell response during antigen challenge.

- **Yisong Wan, Ph.D.**, University of North Carolina, Regulation of Treg function and Foxp3 expression — Wan's group has shown that GATA3, a transcription factor known for its role in Th2 differentiation, is also an important molecule for regulatory T cell (Treg) function. GATA 3 appears to function in Treg cells in part through controlling the expression of a molecule known as Foxp3.

- **Weiguo Zhang, Ph.D.**, Duke University, Transmembrane adaptor proteins in T cell activation and autoimmunity: Zhang has described how two transmembrane adaptor proteins, LAT and LAB, control T cell activation and autoimmunity. He recently showed that LAT is particularly important in the development and function of Treg cells and control of T cell expansion and cytokine production.

- **Lishan Su, Ph.D.**, University of North Carolina, Sanity of host immunity: Foxp3+Treg cells in HIV-1 replication and pathogenesis: Su has developed mice with humanized immune systems, which allows him to use the animals to investigate the roles of Tregs in HIV infection. He showed that although HIV suppresses anti-virus immunity during the early stages of the infection, Tregs suppress HIV-induced immune hyperactivation during the later stages of disease, and thereby slow down disease progression.

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Autoimmune mysteries spark ongoing research

By Josh Zeldin

NIEHS epidemiologist Christine Parks, Ph.D., spoke to employees and guests May 27 on "Autoimmune diseases: What we know (and don't know) about environmental risk factors and why we care." Parks' presentation addressed current knowledge surrounding environmental risk factors for the nearly 80 autoimmune diseases that affect five to eight percent of the population. She also examined why people should care about these risk factors and the impact of these chronic and incurable diseases on the workplace.

The presentation was sponsored by the NIEHS Disability Advocacy Committee (DAC) and hosted by committee co-chairs Dick Sloane and Tina Jones.

At the beginning of her talk, Parks, a research fellow with the NIEHS Chronic Disease Epidemiology Group, said her presentation would try target a general population without a science background. Despite many of the audience lacking this education, the subject of autoimmune diseases was close to the heart of attendees who have either been directly affected by autoimmune diseases or known someone who has been affected. The presentation had added appeal to attendees since Parks herself also has a family history of autoimmune diseases.

Parks' background includes her work on the Carolina Lupus Study. She helped organize a workshop in September 2010 that included panels of experts evaluating the state of the science in autoimmune disease research (see story). She suggested that those interested in understanding more about autoimmune disease visit the Web site of the American Autoimmune Related Diseases Association, a clearinghouse for patient and advocate information. (Photo courtesy of Steve McCaw)

Among scientists attending the presentation was NIEHS biologist Xiao-Ping Yang, Ph.D., of the Institute's Cell Biology Group. (Photo courtesy of Steve McCaw)

Elusive causes of autoimmune disease

After giving a brief introduction of her history and connection to autoimmune disease, Parks dove right into basic facts, subsequently defining autoimmune disease, outlining its known causes, and describing briefly its prevalence in the United States.
While scientists have not been able to pinpoint a single source triggering autoimmune diseases, Parks made it clear that the problem is, in most cases, likely to be due to a mix of both genetic and environmental factors.

"The story is not yet entirely clear," Parks conceded. "Many aspects of these diseases are just not well understood."

This sentiment was echoed throughout the presentation as Parks identified known risk factors for autoimmune diseases, including being a female, family history, ethnicity, cigarette smoking, silica dust, sunlight exposure, infections, ionizing radiation, and solvents. Parks again highlighted how this list included both environmental

and genetic risk factors, underscoring how the causes of these diseases may be exponentially complex and interconnected.

As with cause, the mechanisms of autoimmune disease have proven elusive. While there is research linking autoimmune diseases to T-cell regulation, the aryl hydrocarbon receptor, and toll-like receptors, scientists are still working to understand how these relate to environmental and genetic causes.

Visitors included Pete Schubert, center, from neighboring U.S. Environmental Protection Agency. Seated in the background is DAC co-chair Sloane. (Photo courtesy of Steve McCaw)

Limitations of current research and research methods

After touching on more rudimentary, technical information, Parks transitioned to a less scientific segment of her presentation to identify gaps in the research of autoimmune diseases. Parks stressed that there needs to be more exploration of potential risk factors, such as pesticides, metals, air pollution, and other forms of chemical exposures that affect immune function and inflammatory processes.

Additionally, Parks pointed to the possible influence of psychosocial factors, such as stress — a subject, according to Parks, that hasn't been given sufficient attention. She also pointed to the need for expanding research methods and tools used to investigate risk factors in human studies.

"We do need systematic methods for studying the environment," Parks explained. "We need better tools."

Among the challenges of current epidemiological studies of autoimmune diseases is the need to rely on self-report of past exposures and the lack of resources and attention given to developing validated questionnaires linking self-report to objectively verified measures. Also, according to Parks, the lack of a comprehensive registry base has hampered scientists trying to extrapolate consistent patterns to formulate reasons to explain what seems to be a rising incidence of autoimmune disease.

"Disease rates may be increasing," Parks said, "and we don't know why this is happening."

While the unknown can be challenging, Parks was optimistic about the future of autoimmune disease research — a future she hopes will be marked by more answers and clarification to address a public health problem that costs as much as $100 billion annually in direct medical expense.

"Solutions will come," Parks predicted. "It's just a matter of time, with the growing public awareness and attention of the research community."

(Josh Zeldin is a summer intern with the NIEHS Office of Communication and Public Liaison. He is a student at the University of North Carolina at Chapel Hill.)

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Is spit the future in diagnosis of preclinical Parkinson's?

By Emily Zhou

NIEHS grantee Jing Zhang, M.D., Ph.D., is a scientist on a journey, searching for the Holy Grail of biomarkers for early detection of Parkinson's disease (PD). Zhang, a Shaw Endowed Chair in Neuropathology at the University of Washington School of Medicine, discussed his work in a talk June 3 at NIEHS.

The seminar described Zhang's first-of-its-kind research utilizing proteomics to dissect PD by detecting protein markers in human saliva for early diagnosis and tracking of disease progression. Understanding how to translate bench science discoveries in PD biomarkers to the bedside, where easy and non-invasive sampling is essential, has become a major focus of Zhang's research.

In the clinic of the future, Zhang said, "Spitting could be a standard routine" for sample collection to analyze biomarkers for several neurodegenerative diseases, including PD. He emphasized that mass spectrometry (MS) analysis of proteins can be useful in identifying novel biomarkers, because proteins are functional units, and he argued that saliva maybe the future for early diagnosis because it is easy to collect non-invasively, compared to blood or cerebrospinal fluid (CSF).

NIEHS Scientific Review Administrator Leroy Worth, Ph.D., hosted the talk. NIEHS has made several training and research grants to Zhang, who joked, "EHS is my host institution," because of its long-term support for his research. (Photo courtesy of Steve McCaw)

Biomarker discovery for PD using proteomics by MS

Due to the limitations of dopamine (DA) imaging (see text box), Zhang turned to genomics and metabolomics approaches in his quest for the ideal PD biomarkers. He found, however, that results from these studies were difficult to replicate, partly because of the heterogeneity of human samples and technical difficulties.

Instead, Zhang's laboratory now uses a proteomics platform utilizing MS and refined quantification methods. As he pointed out, "The take home message of MS is that the absence of a protein in an MS analysis only means that it is not detected, not that it's absent."

Zhang picked isotope-labeling technology to better quantify proteins from an MS peak due to its advantage in detection with less abundant proteins and higher quantitative precision. In addition, he and his colleagues utilized a subproteome analysis to examine proteins in discrete neuronal populations and cellular constituents, such as substantia nigra pars compacta, middle frontal cortex, and Lewy bodies. As a result, the group discovered 400 proteins that were altered in abundance in response to the presence and severity of PD.

Early in his talk, Zhang said, "Many [researchers] get discouraged with omics studies, because of low reproducibility." However, he said, "[Although] the overlapping of precise targets from omics studies is low, the overlap of pathways [such as mitochondrial dysfunction, oxidative stress, and inflammation] is highly consistent." (Photo courtesy of Steve McCaw)

Validation — the critical test for biomarkers

To verify candidate biomarkers, Zhang utilized Luminex technology to analyze multiple proteins. This technology allows the coating of beads with different fluorescent tags. The coating of the captured antibody pinpoints the identity of the analyte, while a second laser/detector records abundance. Using a combination of different markers for PD diagnosis, progression, and severity, Zhang said he was able to achieve 95 percent specificity and sensitivity. Two major issues he emphasized during the seminar were the utilization of independent cohorts and inclusion of disease control groups for validation studies.

Saliva as the source for preclinical diagnosis of PD

According to Zhang, although most researchers consider CSF the most informative specimen, collection involves extraction of fluid from the spine, a procedure most patients are reluctant to undergo for screening purposes. Blood-based biomarkers have major limitations, especially when a proteomics approach is used, and targeted searches have had limited success to date.

Therefore, Zhang turned to saliva, most of which is produced by the submandibular gland. This gland is regulated by the sympathetic and parasympathetic nervous systems, and, Zhang said, Lewy body pathology in PD patients can be detected in saliva even before patients manifest symptoms.

Along with staff from the NIEHS Division of Extramural Research and Training, scientists from other divisions also wanted to hear Zhang's talk. Shown above, NIEHS Division of Intramural Research epidemiologist Honglei Chen, Ph.D., above, who studies risk factor associations for PD, ponders the potential of non-invasive early detection. (Photo courtesy of Steve McCaw)

"The future of preclinical diagnosis [of PD] could be in saliva," concluded Zhang. "Saliva could be useful for [screening] vulnerable populations at high risk for PD, such as those with autonomic failure, heart denervation, constipation, depression, and disorders of olfaction."

(Emily Zhou, Ph.D., is a research fellow in the NIEHS Laboratory of Signal Transduction Inositol Signaling Group.)

PD and current methods of diagnosis

PD is the most serious movement disorder afflicting millions of Americans. Pathological hallmarks of PD are loss of dopaminergic neurons in the substantia nigra with resultant depletion of DA and the presence of Lewy bodies in the remaining neurons. Currently, DA imaging is the gold standard biomarker for PD diagnosis, and it could also provide early diagnosis of parkinsonism. "Even at early clinical stages, a majority of DA is already lost," said Zhang.

However, differentiating PD from other parkinsonian disorders, including multiple system atrophy and progressive supra-nuclear palsy, cannot be readily achieved by DA imaging. DA imaging is also subject to the influence of medications, which makes it difficult to monitor disease progression with this method.

As Zhang explained, "DA imaging, in addition to cost and accessibility, is only a surrogate biomarker, which does not point to any pathological mechanism of PD." According to Zhang, quite a few other movement disorders mimic PD clinically, making an accurate diagnosis of PD often difficult even in the best hands. Finally, the natural course of PD varies substantially, with most patients developing first mild cognitive impairment and then dementia as the disease progresses.

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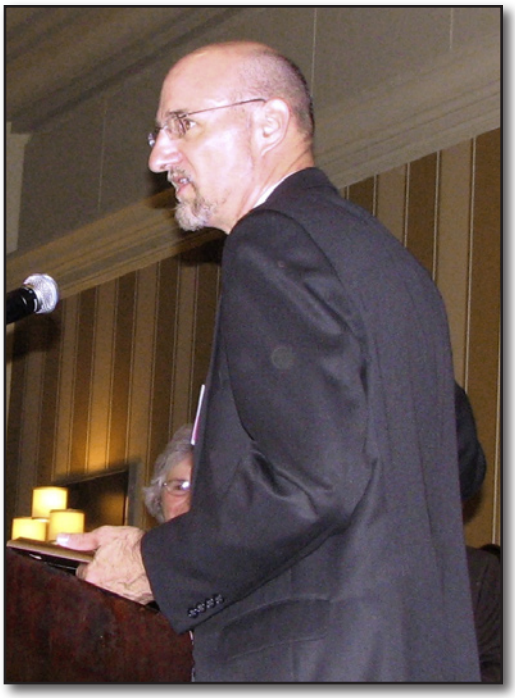
Copeland chairs mitochondrial disease symposium

By Jeffrey D. Stumpf

As the importance of environmental health has been magnified in the treatment of mitochondrial diseases, NIEHS has teamed up with the United Mitochondrial Disease Foundation (UMDF) to showcase research about mitochondrial toxicity to researchers, clinicians, and patients. To that end, NIEHS Laboratory of Molecular Carcinogenesis Acting Chief Bill Copeland, Ph.D., chaired the 2011 UMDF symposium in Schaumburg, Ill., that featured presentations by several NIEHS intramural researchers and grantees.

Mitochondrial diseases are a set of many multi-systemic diseases that result in debilitating and life-threatening symptoms, including extreme muscle fatigue, exercise intolerance, paralysis, and organ failure. These diseases may be fatal to infants, as well as go unnoticed until middle-aged adulthood. The symposium showcased research on mitochondrial and nuclear DNA disease-causing mutations, mechanisms for disease, and functions of mitochondria in diabetes. Researchers estimate that as many 1 in 2000 people may have a mitochondrial disorder, though many are poorly diagnosed.

UMDF was created in 1996, with the goal of promoting research and education in mitochondrial disorders, along with providing support to those affected. Since its foundation, UMDF has funded more than $7 million for research in the hope of improving diagnosis and treatment, as well as developing a cure for mitochondrial disease.



Copeland, shown speaking at the symposium, has been a tireless advocate for people with mitochondrial disease. These diseases are often under-diagnosed or dismissed as too rare to attract substantial research investment. (Photo courtesy of UMDF)

Putting the 'E' in UMDF

In addition to chairing the symposium, Copeland organized a session on mitochondrial toxicity. The session discussed environmental effects on mitochondrial diseases because pharmaceutical and environmental toxins often initially compromise mitochondrial function. "It has become apparent that the mitochondria is the 'canary in the coal mine' for the cell," Copeland said.

The mitochondrial toxicity session highlighted a multifaceted approach in talks from clinicians, industry, and academic researchers. Former NIEHS postdoctoral trainee and current NIEHS grantee, Joel Meyer, Ph.D., discussed his lab's research studying how mitochondrial DNA damage in the nematode *C. elegans* can be cleared by the natural turnover of mitochondria.

"Mitochondrial DNA is much more sensitive than nuclear DNA to many environmental genotoxins and, in many cases, the damage cannot be repaired," Meyer explained. "If mitochondrial dynamics is an important means of removing such damage, then people with impaired mitochondrial dynamics would be at greater risk."

Meyer is an assistant professor of environmental toxicology at Duke University, where he earned his Ph.D. in 2003. (Photo courtesy of Duke University)

NIEHS intramural research was also represented by abstract talks and poster presentations by the Mitochondrial DNA Replication Group, led by Copeland. The subjects of this research ranged from mouse and yeast models of mitochondrial dysfunction, to biochemical mechanisms of mitochondrial replication and disease.

"The goal of our group's research is to understand the origin of mutations in the mitochondrial DNA that cause disease," noted Copeland. "We are trying to understand how disease mutations in mitochondrial replication genes ameliorate normal DNA replication."

Another former NIEHS trainee and current grantee, Miguel Garcia-Diaz, Ph.D., was awarded a research grant for his future studies in mitochondrial transcription. Being a private foundation, UMDF awards grant money received from numerous fundraisers to researchers who propose important mitochondrial research. As Garcia-Diaz pointed out, the awards are necessary for expanding studies on pathogenic mechanisms of mitochondrial disorders.

"The award will provide funds to initiate the study of tRNA maturation in mitochondria," said Garcia-Diaz. "Some of these processes have been associated with mitochondrial diseases and are thought to be affected by environmental exposures."

Garcia-Diaz is an assistant professor of pharmacological sciences at Stony Brook University. (Photo courtesy of Miguel Garcia-Diaz)

(Jeffrey Stumpf, Ph.D., is a postdoctoral fellow in the NIEHS Laboratory of Molecular Genetics Mitochondrial DNA Replication Group.)

Copeland recognized for service to the mitochondrial disease community

In addition to leading the mitochondrial DNA replication group, Bill Copeland, Ph.D. served as the UMDF Grant Review Committee Co-chairman and chairman from 2004-2008. Copeland continues to chair the UMDF research Policy Review Committee in addition to serving on the Scientific and Medical Advisory Board. He has been serving on the symposium planning committee for four years, including being 2011 Scientific Course Chair.

"Throughout the continuing tenure with the UMDF in various capacities, Dr. Copeland has been extremely knowledgeable, helpful, encouraging, and accessible," commented UMDF CEO/Executive Director Charles Mohan. "He is a real favorite among the UMDF administration and staff and we look forward to an ongoing relationship with Dr. Copeland for many years to come."

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Superfund postdoc unravels arsenic exposure

By Melissa Kerr

Arsenic exposure does not have to be in large doses in order to have severe damaging effects on a biological system, according to Courtney Kozul-Horvath, Ph.D., a Superfund Research Program trainee at Dartmouth Medical School who discussed her research June 17 at NIEHS. Kozul-Horvath became intrigued with the effects of environmental exposure to low doses of arsenic during her graduate work at Dartmouth, and she continues to investigate the threat of exposure to this dangerous metalloid on public health worldwide.

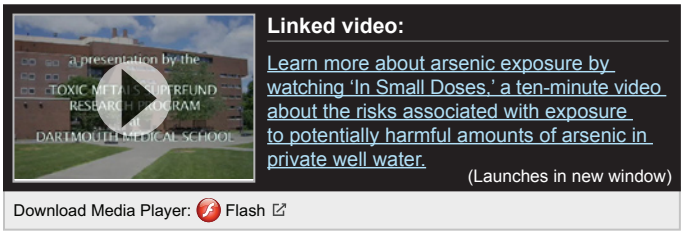
Kozul-Horvath discussed her findings in a presentation titled "Developmental and Immunological Effects of Low Dose Arsenic Exposure in Mice." (Photo courtesy of Jennifer Weinberg)

Arsenic in the United States

Arsenic is a naturally occurring element and can also enter drinking water as a by-product of agricultural and industrial activities. Human exposure to arsenic has resulted in a variety of health effects that include cancer of the lungs, skin, and liver. Kozul-Horvath cited a 2006 article published in Environmental Health Perspectives that described arsenic as the "liquid path to lung disease."

Because of the health effects caused by arsenic, in January 2006 the Environmental Protection Agency (EPA) lowered the acceptable level of arsenic in drinking water from 50 parts per billion (ppb) to 10 ppb.

Kozul-Horvath works in New Hampshire, which is also known as the "Arsenic State," and one of her earlier projects was an education video for people who rely on well water in parts of New England where arsenic levels are a threat to their health.



"This is a problem because as much as 50 percent of the population in New Hampshire and Maine get their water from private wells, which are not regulated," she explained. Within this region, the typical level of arsenic found in private wells ranges from 1 to 100 ppb.

Bethesda, Md.-based NIEHS Legislative Liaison Mary Gant happened to be on campus and made a point of attending the talk. (Photo courtesy of Jennifer Weinberg)

Arsenic in the lungs

"One of the hypotheses that I have been beating around for the last four years or so is that perhaps arsenic is able to elicit such a variety of different health effects, because maybe it affects the immune system," Kozul-Horvath said.

Kozul-Horvath's research team set up a study where two sets of mice were infected with a mouse-specific strain of H1N1 influenza virus. The mice were divided into two groups. One group was infected only with H1N1. The other group was exposed to 100 ppb of arsenic in their drinking water and then infected with H1N1.

The researchers found that the arsenic-exposed mice, although they were exposed to the same level of flu, had about 10-fold more of the virus in their lungs. Early in the infection, arsenic-exposed mice had no immune response to major infection of virus. Later in the infection, there is an overabundant response that leads to hemorrhaging within the lung.

"This tells us that these [CD8] cells in the arsenic-exposed mice are not functioning to clear the virus properly," Kozul-Horvath explained.

Arsenic exposure during early development

In the next phase of experiments, Kozul-Horvath and her team were interested in attempting to discern roles of arsenic exposure on the development of the immune response. This time using the EPA standard of 10 ppb, the research team used four mice groups: mice that have never been given arsenic, mice that are only exposed to arsenic during the postnatal period, mice that only experience arsenic exposure during the *in utero* period, and mice receiving arsenic during their entire developmental period. The results showed that the growth rate of the mice was significantly affected, regardless of when they were exposed, with females more affected than males.

Kozul-Horvath looks forward to continuing to determine the roles that low-levels of arsenic play in the development of the immune system. She would also like to explore further how arsenic exposure changes the immune system response to an infection of influenza.

"We keep lowering and lowering our dose, figuring that eventually we are going to bottom out and not see an effect, but we're just surprised one time after another by the types of things that we see in this model," she concluded.

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

NIEHS/NTP Director Linda Birnbaum, Ph.D., doesn't get to as many talks as she'd like, but she wasn't about miss this one on arsenic and windows of susceptibility. Birnbaum had several questions for Kozul-Horvath about her future plans. (Photo courtesy of Jennifer Weinberg)

NIEHS Health Scientist Administrator Heather Henry, Ph.D., joined several other members of the SRP at the presentation. (Photo courtesy of Jennifer Weinberg)

An impressive list of honors and awards

Although Kozul-Horvath is still a young scientist, she has already been the recipient of several awards and commendations. The list includes awards from the Women in Toxicology Scholarship Fund, the Northeast Society of Toxicology, Molecular Biology Specialty Section, "Best Student Poster" at the Superfund Research Program's annual meetings in 2007 and 2008, various awards from the Society of Toxicology, and the "Outstanding Oral Presentation" award from the International Central and Eastern European Conference on Health and the Environment in 2008.

Just this past year, she was the recipient of NIEHS's annual award presented in honor of Karen Wetterhahn, Ph.D. (see story). Wetterhahn was a leader in heavy metals research who died in 1997 as a result of a lab accident. Kozul-Horvath exemplifies the qualities of scientific excellence the Wetterhahn award was designed to honor.

She is also a Ruth Kirschstein National Research Service Award fellowship awardee.

NIEHS Principal Investigator Mike Waalkes, Ph.D., was literally on the edge of his seat as Kozul-Horvath described her data. Waalkes, who heads the NTP Inorganic Carcinogenesis Branch, is the author of what has been described as one of the three most important recent papers about arsenic. (Photo courtesy of Jennifer Weinberg)

Kozul-Horvath joined the host of her lecture, SRP Director Bill Suk, Ph.D., left, on the patio outside the NIEHS main building. (Photo courtesy of Jennifer Weinberg)

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NIEHS at Society for In Vitro Biology meeting

By Eddy Ball

NIEHS scientists contributed their bioinformatics expertise to a weeklong annual meeting of the Society for In Vitro Biology June 4-8 in Raleigh. They joined hundreds of plant and animal biologists from the government, academia, nonprofit, and private sectors for a discussion of topics ranging from proof-of-principle research to product development.

Symposium conveners Bushel, smiling in background left, and Li, foreground, listened to and sometimes laughed along with presenters. Not shown are fellow conveners Lia Campbell, Ph.D., director of research at Cell and Tissue Systems, Inc., and Prakash Lakshmanan, Ph.D., lead for the molecular breeding program at the David North Plant Research Centre. (Photo courtesy of Steve McCaw)

NIEHS Biostatistics Branch Principal Investigator Leping Li, Ph.D., and Staff Scientist Pierre Bushel, Ph.D., served as conveners of the plenary symposium "Bioinformatics/Statistics in Research and Product Improvement" featuring presentations on the power of bioinformatics discovery in agronomy, embryonic stem cell biology, and cancer. Former NIEHS Biostatistics Branch Visiting Fellow Sailu Yellaboina, Ph.D., (see story) gave one of the three presentations at the symposium.

As the symposium organizers maintain, data from microarrays, next generation sequencing, and single nucleotide polymorphism analysis continue to proliferate, leading to "the need to integrate these data sets and analysis results for a more informed interpretation of biological consequences and phenotypic events."

Looking at the end result

The opening talk of the session was presented by research agronomist Mei Guo, Ph.D., of DuPont's Pioneer Hi-Bred International, a producer of genetically engineered crops to improve yield and hardiness, as well as provide greater insect and disease resistance. While she focused more on genetic engineering than on the bioinformatics of candidate gene discovery, the dramatic results of her research underscored the important role of bioinformatics in helping select candidate genes.

Guo showed photos illustrating the dramatic variation in size among vegetable strains. Her group manipulates candidate genes with the goal of increasing crop output. (Photo courtesy of Steve McCaw)

Guo's team manipulated expression of two cell number regulator (CNR) genes in corn, downregulating ZmCNR01 and overexpressing ZmCNR02, to increase the stalk height, overall biomass, and number of kernels on each ear by as much as 20 percent. Guo noted that each addition kernel ring on an ear of corn increases per acre yield by at least five percent.

Investigating genes involved in embryonic stem cell maintenance

As Yellaboina explained when he began his talk, "ES (embryonic stem) cell therapies have been proposed for regenerative medicine and tissue replacement after injury or disease," because these cells maintain an epigenetic state that enables both self-renewal and differentiation into any of the cellular systems of the adult body. However, he pointed out, in order to utilize their remarkable properties, scientists need to better understand the genes essential for the self-renewal and pluripotency and how to manipulate them to influence the timing and direction of ES cell differentiation.

According to Yellaboina, some 400 genes have been identified in previous genome-wide screenings as playing a role in maintenance of ES cell identify. "We undertook a massive effort to integrate approximately 30 previously published gene expression microarray datasets in mouse ES cells and differentiated cells across various developmental stages," he explained. The researchers used a meta-analysis approach to rank all the genes in order of their likelihood to be required for ES cell maintenance and performed RNA interference screens to examine 25 previously unscreened genes ranked in the top 500.

Although he conceded, "the picture of self-renewal still remains largely incomplete," the group has developed a systematic approach to gain systems-level understanding of ES cell maintenance.

Yellaboina was making his final presentation as an NIEHS postdoc. In mid June, he left for a post at the C.R. Rao Advanced Institute of Mathematics, Statistics, and Computer Sciences in his native India. (Photo courtesy of Steve McCaw)

An integrated approach to studying epigenetics

The final speaker at the symposium was computational biologist Guo-Cheng Yuan, Ph.D., an assistant professor at the Harvard School of Public Health and Dana-Farber Cancer Institute.

As Yuan said at the beginning of his talk, epigenetic alterations are the result of several discrete factors working in concert. Insights into Polycomb group (PcG) genes targeting mechanisms that promote histone trimethylation in mammals may help scientists better understand how stem cell identity is maintained.

Yuan reported on the analysis of genome-wide ChIP-chip data on several PcGs related to epigenetic modification, explaining that changes in PcG targeting patterns are well coordinated with alterations in gene expression. Yuan also said that his model performs well and over 90 percent of the top 400 predicted genes were correct targets and that the genes that have high prediction scores tend to be associated with H3K27me3 in multiple cell lines.

Yuan's group develops statistical and computational methodologies for genomic data analysis and integration, with the aim of characterizing systems-level gene regulatory mechanisms. (Photo courtesy of Steve McCaw)

As scientists discussed their research inside, a statue of Sir Walter Raleigh in front of the Raleigh Convention Center showed the city's support for the Susan G. Komen Race for the Cure taking place the following weekend. (Photo courtesy of Steve McCaw)

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The presenters and their collaborators

Abstracts for the talks in the bioinformatics plenary symposium have been posted online by the Society for In Vitro Biology.

- PS-7 Utilizing Bioinformatics in Identification and Functional Analysis of Cell Number Regulator Genes in Diverse Plant Species for Crop Improvement of Maize – A Whole Different Animal. Mei Guo, Mary A. Rupe, Jo Ann Dieter, Jijun Zou, Daniel Spielbauer, Keith E. Duncan, Richard J. Howard, Zhenglin Hou, and Carl R. Simmons. Pioneer Hi-Bred, A DuPont Business, Johnston, Iowa, and DuPont Crop Genetics Research, Wilmington, Del. Email: mei.guo@pioneer.com
- PS-8 Integrating Genomic Datasets to Understand the Mechanisms of Embryonic Stem Cell Maintenance. Sailu Yellaboina, Xiaofeng Zheng, Dmitri Zaykin, Guang Hu, and Raja Jothi. Biostatistics Branch and Laboratory of Molecular Carcinogenesis, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, N.C. 27709. Email: yellaboinas@mail.nih.gov
- PS-9 Query of Polycomb Targeting Mechanism in Mammals by Integration of Experimental and Computational Methods. Guo-Cheng Yuan. Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute and Department of Biostatistics, Harvard School of Public Health. Email: gcyuan@jimmy.harvard.edu

NIEHS trainee wows Science Café audience

By Eddy Ball

Postdoctoral fellow Jeffrey Stumpf, Ph.D., presented an engaging introduction to DNA before a capacity audience at Raleigh's latest Science Café June 22.

Stumpf spoke without slides or notes to some 100 attendees, ranging from a contingent of fellow NIEHS scientists to people with limited backgrounds in science and even some of their children, gathered in an informal venue at Raleigh's Irregardless Café to satisfy their appetites for good food and new information about science. The enthusiastic audience gave Stumpf several rounds of applause, enjoyed his humor, and took full advantage of an extended question-and-answer session at the end.

In a note afterwards to Stumpf, above, event organizer Katey Ahmann, of the N.C. Department of Environment and Natural Resources (DENR), wrote, "You did a great job and I have received many comments on how much people enjoyed your presentation and the café in general." (Photo courtesy of Alan Neifeld)

Before the talk got underway, not a seat was empty as the audience, ranging in age from 8 to 80, enjoyed dinner and conversation while waiting for the talk to begin. (Photo courtesy of Alan Neifeld)

Communicating science to the community

Stumpf is a member of the NIEHS Mitochondrial DNA Replication Group in the Laboratory of Molecular Genetics (LMG) headed by Principal Investigator and LMG Acting Chief Bill Copeland, Ph.D. Along with his scientific research, Stumpf is involved in career development activities, including communicating science to more general audiences through outreach activities in schools and community settings, and writing about science for the Environmental Factor newsletter (see story).

This audience member holds a microphone as he waits his turn to ask Stumpf a question. DENR technicians record the Science Café talks, which are available afterwards online as podcasts and, by special request, in transcripts. (Photo courtesy of Alan Neifeld)

As he began his talk, Stumpf remarked on the burgeoning interest among journalists and the general public about DNA research. "It's something that's really hitting all the non-scientists out there," he said. "It's very important that, as scientists, we get the information out to the public about what we are doing, and how we're trying to improve medical science and human health."

Stumpf used several down-to-earth metaphors and humorous analogies to hook his audience, and he took full advantage of the sensational statistics about DNA function and replication to keep his listeners' attention. He described the double helix as twisted railroad tracks, compared repairing DNA breaks to coping with the stress response from an overbearing and demanding mother in law, and amazed the audience with the sheer magnitude of the genome.

"There are 3.3 billion base pairs in every one of your cells," Stumpf explained. "With most of us having 10 to the 13th [10 trillion] cells in our bodies, that means that if you strung every piece of DNA one by one, you'd be able to do 67 round trip travels to the sun from the earth." Turning to DNA replication, he added more fuel to his presentation. "The DNA polymerase makes about one mistake per 100,000 base pairs, and that's pretty impressive, except that there's about 3.3 billion base pairs in a genome. So you're looking at about 30,000 mistakes in replication."

Stumpf also talked briefly about the advantages of bacteria and yeast models for studying genetics, as well as some mouse models of mitochondrial DNA mutations involved in aging and disease. But with a sense of his audience's interests in how genetics research will impact their lives, toward the end of his talk, he moved away from his expertise and out of his comfort zone of basic genetic research and microbiology, into the potential for translation of research findings into drug development, personalized medicine, and targeted therapies, which sparked even more audience interest and raised a few questions that Stumpf had to concede that he just couldn't answer.

Founded in 2006, Raleigh's Science Café series is sponsored by the North Carolina Museum of Natural Sciences and the scientific research society Sigma Xi for communicating science to the public. The series, which is part of a national movement in the U.S., features monthly talks by scientists of nearly every specialty to give citizens access to scientific developments and face-to-face contact with scientists at the community level in informal settings, such as restaurants, coffee shops, and taverns.

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Paper from Dudek group highlighted by Faculty of 1000

By Eddy Ball

A new paper from a team of researchers led by NIEHS Principal Investigator Serena Dudek, Ph.D., has been singled out for commendation by the Faculty of 1000 (F1000). The study, which details the mechanism underlying rapid transcription of immediate early genes (IEGs) in neurons, appeared online in the journal Nature Neuroscience in May (see story).

First author on the paper, Visiting Fellow Ramendra Saha, Ph.D., is a member of the Synaptic and Developmental Plasticity Group headed by Dudek in the NIEHS Laboratory of Neurobiology. NIEHS Principal Investigator Karen Adelman, Ph.D., head of the Transcriptional Responses to the Environment Group in the Laboratory of Molecular Carcinogenesis, is a co-author on the paper who made important contributions to the study design.

Dudek has devoted her career to seeking the answers to questions about synaptic plasticity and its role in learning, behavior, and development. (Photo courtesy of Steve McCaw)

A groundbreaking paper with exciting results

F1000 evaluators Jeremy Day, Ph.D., and David Sweatt, Ph.D., of the University of Alabama at Birmingham, wrote in their review, "This article elegantly examines the contribution of RNA polymerase II (Pol II) stalling to stimulus-induced gene expression in neurons, revealing that polymerase stalling is a common mechanism by which immediate early genes (IEGs) are poised for rapid transcription in response to neuronal events."

Although Day and Sweatt acknowledge that further research is needed to determine the precise role of rapid transcription of IEGs in behavioral memory and neuronal plasticity, they concluded, "These exciting results… represent a breakthrough in our understanding of transcriptional control of gene expression in the brain."

Evaluating top publications

F1000 is a post-publication review group of thousands of experts worldwide who identify and evaluate the most important articles in biology and medical research publications. The selection process comprises a peer-nominated global faculty of the world's leading scientists and clinicians who rate the best of the articles they read and explain their importance in approximately 1,500 reviews each month.

Citation: Saha RN, Wissink EM, Bailey ER, Zhao M, Fargo DC, Hwang JY, Daigle KR, Fenn JD, Adelman K, Dudek SM. 2011. Rapid activity-induced transcription of Arc and other IEGs relies on poised RNA polymerase II. Nat Neurosci; doi:10.1038/nn.2839: [Online 29 May 2011].

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Saha worked with Dudek and Adelman on a new integrative approach to understanding transcription in neurons. (Photo courtesy of Steve McCaw)

Adelman's group investigates the dynamic interplay between signals from the environment and transcription by RNA Pol II. (Photo courtesy of Steve McCaw)

NIEHS nano consortium meets for progress updates

By Thaddeus Schug

Members of the NIEHS nanotechnology consortium gathered at the University of Washington School of Medicine in Seattle, June 15-16 for the second official meeting of the group to cover research progress updates and hold a meeting for the Steering Committee. The NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium Meeting offered an opportunity for grantees from NIEHS programs, including Nano Grand Opportunities (NanoGO), Challenge Grant, Outstanding New Environmental Scientist (ONES), and Research Project Grant (R01), to share and integrate data.

Sri Nadadur, Ph.D., the meeting organizer and the health scientist administrator at NIEHS who oversees much of the Institute's portfolio on nanomaterials in health and safety, said of the

Shown left to right, Chris Wingard, Ph.D., Tim Fennell, Ph.D., and Apparao Rao, Ph.D., discuss nanomaterial health and safety during the poster session on day one. (Photo Courtesy of Elena Reitman)

programs, "We are beginning to see progress in both the individual research projects and in meeting the overall goals of the consortium." Nadadur added, "This group of scientists provides a wide range of expertise for us to investigate the unknown health and safety implications associated with nanomaterials."

Nadadur, left, graduate student David Scoville, center, and Terry Kavanagh, Ph.D., talked during the poster session. Kavanagh, who studies the risks associated with quantum dot exposure, hosted the meeting at the newly renovated University of Washington Medical Campus. (Photo Courtesy of Elena Reitman)

Use and applications on the rise

Engineered nanomaterials (ENMs) represent a significant breakthrough in material design and development for medicine, industry, and consumer products. According to experts at the meeting, global demand for nanomaterials and nano-enabled devices is estimated to approach $3.1 trillion by 2015. This increased production provides expanded opportunities for exposures, with unknown health consequences that are critical for scientists to better understand.

Jerry Heindel, Ph.D., acting chief of the Cellular, Organs, and Systems Pathobiology Branch of the NIEHS Division of Extramural Research and Training, opened the meeting by stating, "NIEHS has provided a tremendous opportunity for investigators to work together to solve complicated issues that could not be addressed in individual research laboratories." Heindel added, "We are relying on you to pool together your resources and brain power and to work as a team so that we can better understand nanomaterial health and safety."

David Eaton, Ph.D., left, and Terry Gordon, right, interact during one of several discussion sessions. (Photo Courtesy of Elena Reitman)

During the two-day meeting, consortium scientists presented brief updates on their individual program projects, while focusing on their collaborative efforts within the consortium. Presentations were also given by Scott McNeal, Ph.D., of the Nanotechnology Characterization Lab (NCL), which is providing expertise on the characterization of ENMs investigated by the centers, and Jeffery Zink, Ph.D., a principal investigator in the University of California, Los Angeles scientific core. Day one concluded with a poster session featuring displays from graduate students, postdocs, and other members of the Environmental Sciences Nano Consortium.

A major portion of day two was dedicated for Steering Committee deliberations to identify common areas of research involving the ENMs and risk assessment systems being investigated by the consortium. Steering Committee deliberations will continue through monthly conference calls to further focus consortium efforts on identifying physical and chemical properties of ENMs, as well as their implications for human health. Also participating in the meeting were members of the External Advisory Committee, and Program Advisory Scientists. The next face-to-face meeting of the NCNHIR consortiums will be held at NIEHS during the winter of 2011-12.

(Thaddeus Schug, Ph.D., is a postdoctoral research fellow in the NIEHS Laboratory of Signal Transduction and a regular contributor to the Environmental Factor. He is currently on detail as a program analyst in the NIEHS Division of Extramural Research and Training.)

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NIEHS-funded study suggests high infant exposure to flame retardants

By Archana Dhasarathy

A new NIEHS-funded study by chemist Heather Stapleton, Ph.D., and her colleagues indicates that infants are being exposed to chemical flame retardants found in up to eighty percent of commonly used baby products, including car seats. According to Stapleton, these chemicals may be absorbed by infants through inhalation, ingestion or via their skin, and may pose significant health risks during childhood development.

Stapleton, a chemist at the Nicholas School of the Environment at Duke University, was the recipient of the prestigious 2008 NIEHS Outstanding New Environmental Scientist (ONES) award. (Photo courtesy of Steve McCaw)

Stapleton is an assistant professor of environmental chemistry at Duke University. She is an NIEHS Outstanding New Environmental Scientist awardee, and her study was supported by a grant from NIEHS to investigate "Children's Exposure to Flame Retardants: Effects on Thyroid Hormone Regulation."

From furniture to babies

Manufacturers add flame retardant chemicals to polyurethane foam in order to meet a California flammability standard (TB 117) adopted in 1975, which requires it to withstand a 12-second open flame. Furniture manufacturers in many states have adopted the use of flame retardants to comply with the California standard, even though no federal law requires the use of flame retardants.

A few years ago, Stapleton's team was testing some polyurethane foam collected from furniture items that contained a label indicating that they met the California foam flammability standard. When Stapleton was shopping for baby products for her first child, she was surprised to observe the same labels on a number of baby products. "After talking with a few of my colleagues about this, we decided to conduct a study to determine whether and how frequently these items were treated with flame retardants," she said.

Eighty percent of baby products contain flame retardants

In their study, the researchers examined 101 commonly used baby products, including car seats, baby changing pads, and nursing pillows, for the presence of these chemicals. Using mass spectrometry, they confirmed that nearly 80 of these samples contained either a chlorinated or brominated flame retardant additive.

During their analysis they found compounds commonly associated with pentabromodiphenyl ether (pentaBDE), which was banned in Europe and withdrawn from the US market, in five products, suggesting products with pentaBDE are still in use. In addition they found two potential carcinogens, TCEP and TDCPP, and identified two previously undocumented chlorinated organophosphate flame retardants, among others.

Birnbaum has published several studies on flame retardants and is recognized as a leading authority in the field. (Photo courtesy of Steve McCaw)

Health concerns during early infant development

When asked about the exposure and health concerns for infants, Stapleton said, "I don't think we know much at all about the potential human health effects from exposure to these chemicals. What we do know is that infants are likely receiving more exposure to these chemicals than adults. Therefore, more research is warranted to determine if this exposure is leading to any adverse health effects."

NIEHS/NTP Director Linda Birnbaum, Ph.D. concurred. "Some of these chemicals are very persistent in the environment and thus have the potential to cause a variety of adverse health effects," she said. She also pointed out that there are ongoing studies at NIEHS and the NTP that aim to test both short- and long-term effects of a variety of flame retardants.

Avoiding products with flame retardants

Why do we need these chemicals at all, if the law does not require their use and they may be harmful? "Part of the reason to use these chemicals came from the old days, when people smoked a lot," said Birnbaum. Smoking has decreased in recent years, but these chemicals still continue to be used.

So how do parents avoid buying products with flame retardants? Unfortunately, they can't. "The consumer is unable to determine whether a product contains flame retardants or not, as labeling is not required. However, if a baby product contains polyurethane foam, AND a label indicating it meets CA TB 117, there is a very high probability that it will contain halogenated flame retardant chemicals," said Stapleton.

Banned flame retardants resurface

Many flame retardants were used in the 1970s in a variety of children's products, such as child car seats, mattresses, and clothing to reduce deaths from fire. Some of these were subsequently banned due to health concerns. For instance, brominated tris (tris [2,3-dibromopropyl] phosphate] was banned from children's pajamas after it was found to be mutagenic and was shown to be absorbed into children's bodies.

The fire retardant pentabromodiphenyl ether (pentaBDE) can accumulate in humans, animals and the environment and has the potential to cause adverse health effects. In 2003, legislation banning the use of pentaBDE came into existence in the European Union and several states in the U.S.

In Stapleton's study, the researchers found several compounds, similar to those that were banned in pajamas, still present in the products they studied.

In the meantime, Stapleton urged parents with concerns about their children's exposure to these chemicals to write to legislators, and the U.S. Consumer Product Safety Commission, requesting more testing to determine the extent of exposure to these chemicals and to determine if there are any health effects.

(Archana Dhasarathy, Ph.D., is a postdoctoral fellow in the Eukaryotic Transcriptional Regulation Group in the NIEHS Laboratory of Molecular Carcinogenesis.)

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This month in EHP

By Eddy Ball

http://twitter.com/ehponline

Anchored by an image of the devastation at Japan's east coast, the Focus feature story of the July Environmental Health Perspectives (EHP) examines the chemical aftermath following the March 2011 Tohoku earthquake and tsunami. This article discusses current efforts under way to characterize industrial chemical releases following the disaster, and to limit and prevent exposures to hazardous substances.

A second news story, "Phosphorus Recovery: New Approaches to Extending the Life Cycle," looks at some of the novel methods researchers are using to recapture phosphorus from animal and human waste. These methods can augment current sources of phosphorus — which by some estimates are in danger of being depleted — as well as mitigate water pollution by diverting the mineral from runoff.

In this month's Researcher's Perspective podcast, journalists Lizzie Grossman and Winnie Bird tell host Ashley Ahearn what it was like to cover the Tohoku earthquake and tsunami for this month's Focus feature story.

Featured research in the July EHP includes the following:

- "Environmental Lessons from China"
- "Dietary Intervention to Reduce BPA and DEHP"
- "Thyroid Cancers in Ukraine after the Chornobyl Accident"
- "PCBs and IVF Outcomes"
- "Air Pollution and Low Birth Weight"

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Extramural papers of the month

By Jerry Phelps

Read the current Superfund Research Program Research Brief. New issues are published on the first Wednesday of each month.

Prenatal PAH exposure linked to behavioral problems in kids

Children of expectant mothers who are exposed during pregnancy to polycyclic aromatic hydrocarbons (PAH) are more likely to have behavioral problems as they grow and develop. A new study, funded by NIEHS at the Columbia Center for Children's Environmental Health, examined 215 children enrolled at birth. Children with high levels of PAH-DNA adducts, a biomarker of exposure, had more symptoms of attention problems and anxiety at ages 5 and 7 than did children with lower exposure.

PAH exposure occurs as a result of the incomplete combustion of fossil fuels and other organic material. These pollutants cross the placenta during pregnancy and bind to the DNA of the fetus. The researchers measured PAH-DNA adducts in white blood cells from umbilical cord blood samples taken at birth. A few years later, their mothers completed a detailed behavioral assessment of each child.

This study is the first to link behavioral effects with prenatal exposure to air pollution. The results are concerning since attention problems and anxiety may affect subsequent academic performance and social wellbeing.

Citation: Perera FP, Wang S, Vishnevetsky J, Zhang B, Cole KJ, Tang D, Rauh V, Phillips DH. 2011. PAH/Aromatic DNA Adducts in Cord Blood and Behavior Scores in New York City Children. Environ Health Perspect [Online 4 April 2011].

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Breakfast helps to reduce childhood lead poisoning

A first-of-its-kind study of 1,344 children in Jintan, China reports that children who eat breakfast regularly have a blood lead content about 15 percent lower than children who do not. These results are consistent with previous studies in adults, which demonstrated that fasting increases lead absorption from the gut.

The participants took part in the China Jintan Child Cohort Study, which is funded by a grant from NIEHS to the University of Pennsylvania. Children were enrolled in the study in 2004-2005 when they were three to five years old. Their parents filled out questionnaires regarding their eating habits and foods they frequently ate.

The study compared blood lead levels to social factors, eating patterns, and intake of trace minerals and other micronutrients. There were no gender or age differences in breakfast consumption, but there was a marked decrease in blood lead concentration for children who ate breakfast regularly, which was defined as 5 days per week.

The children who ate breakfast regularly had an average blood lead level of 6.1 micrograms/deciliter as compared to 7.2 micrograms/deciliter for those that ate breakfast irregularly.

Citation: Liu J, McCauley L, Compher C, Yan C, Shen X, Needleman H, Pinto-Martin JA. 2011. Regular breakfast and blood lead levels among preschool children. Environ Health 10:28.

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Endoplasmic reticulum stress in obesity

NIEHS-supported scientists at the Harvard School of Public Health report in Nature that abnormal lipid and calcium metabolism are important contributors to endoplasmic reticulum (ER) stress accompanying obesity. These findings suggest that interventions that modulate lipid synthesis or calcium homeostasis might offer new opportunities for treating obesity, insulin resistance, and diabetes.

The ER is the main site of a variety of cellular processes, including protein and lipid synthesis, xenobiotic metabolism, and calcium storage. Disturbances in ER homeostasis can lead to stress and the subsequent activation of the unfolded protein response. Chronic ER stress is known to be important in the development of insulin resistance and diabetes in obese individuals; however, the mechanisms responsible are not well understood.

These investigators compared the proteomic and lipidomic signatures of endoplasmic reticuli purified from the livers of obese and normal sized mice. They observed suppression of protein synthesis and stimulation of lipid synthesis in the ER from the obese mice. Alterations in the fatty acid and fat composition resulted in changes in calcium ATPase activity. They also discovered that correcting the obesity-induced changes in ER phospholipid makeup reduced chronic ER stress and improved glucose homeostasis.

Citation: Fu S, Yang L, Li P, Hofmann O, Dicker L, Hide W, Lin X, Watkins SM, Ivanov AR, Hotamisligil GS. 2011. Aberrant lipid metabolism disrupts calcium homeostasis causing liver endoplasmic reticulum stress in obesity. Nature 473(7348):528-531.

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Astrocytes and microglia display distinct sensitivities to methylmercury

In the first study to compare responses in microglia and astrocytes, the two major forms of glial cells that provide support for neurons in the central nervous system, NIEHS-supported scientists have determined that they react very differently to methylmercury exposure. These findings could be important in the identification and development of therapies to reduce methyl mercury-induced damage to the central nervous system.

Microglia and astrocytes have both been identified as primary targets for the damaging effects of methylmercury. This study was carried out in primary cell cultures of the two cell types to determine their responses to methylmercury exposure with particular attention paid to cell viability, the generation of reactive oxygen species, mercury uptake, and glutathione levels.

The experimental results show that microglia are more sensitive to methylmercury than astrocytes, and they have higher uptake of mercury and lower glutathione levels, which are important in detoxifying reactive oxygen species. Microglia exhibited greater oxidative stress responses to methylmercury exposure than did astrocytes. This study furthers our understanding of how these cell types respond to environmental insults.

Citation: Ni M, Li X, Yin Z, Sidoryk-Węgrzynowicz M, Jiang H, Farina M, Rocha JB, Syversen T, Aschner M. 2011. Comparative study on the response of rat primary astrocytes and microglia to methylmercury toxicity. Glia 59(5):810-820.

(Jerry Phelps is a program analyst in the NIEHS Division of Extramural Research and Training.)

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Intramural papers of the month

By Raluca Dumitru and Ian Thomas

- Diet may protect against mutagens in fried meat
- Formation and repair of double strand breaks in yeast
- Crystal structure-based mutagenesis of EndA nuclease
- A novel protective role for beta2 adrenergic receptor in Parkinson's disease

Diet may protect against mutagens in fried meat

Investigators from NIEHS, along with collaborators from the University of North Carolina at Chapel Hill, the Environmental Protection Agency, and several other institutions, have found that dietary factors can reduce DNA damage caused by heterocylic amines (HCAs), carcinogenic compounds formed in meat cooked at high temperatures.

The researchers determined that eating cruciferous vegetables, such as broccoli and cauliflower, chlorophyll-derived chlorophyllin (CHL) tablets, and yogurt reduced the amount of DNA damage found in colon cells obtained by biopsy, compared to the tissue of other volunteers on a control diet. The study is the first to show that eating these foods can measurably reduce DNA damage in human colon cells.

Sixteen volunteers were divided into two groups of eight. Members of one group were randomly assigned to a diet containing meats cooked at a low (100° C) or high temperatures (250° C). Participants in the other group were randomly assigned to diets containing high-temperature meat alone or in combination with the inhibitors. Within each group, members switched diets after two weeks so that each person could serve as their own control. Blood, urine, and colon biopsies were obtained from participants each week over the four week study.

Urine and fecal samples from the low-temperature meat diet had low levels of mutagenicity, while samples from the high-temperature meat diet displayed significantly increased levels of mutagenicity. Fecal mutagenicity and colon cell DNA damage was significantly decreased in those who added the inhibitors to their diets.

While additional subjects and longer dietary regimens are recommended for future studies, this work establishes an important link between diet and the reduction of DNA damage in the colon.

Citation: Shaughnessy DT, Gangarosa LM, Schliebe B, Umbach DM, Xu Z, Macintosh B, Knize MG, Matthews PP, Swank AE, Sandler RS, Demarini DM, Taylor JA. 2011. Inhibition of fried meat-induced colorectal DNA damage and altered systemic genotoxicity in humans by crucifera, chlorophyllin, and yogurt. PLoS One 6(4):e18707. Story

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Formation and repair of double strand breaks in yeast

A recent NIEHS study is the first to demonstrate that in the budding yeast *Saccharomyces cerevisiae*, single-strand breaks (SSBs) generated by the alkylating agent methyl methanesulfonate (MMS) can lead to double-strand breaks (DSBs) in the DNA of G2/M arrested cells. In addition, the research team identified a novel repair intermediate, called slow-moving DNA (SMD), using pulsed field gel electrophoresis (PFGE). Until the publication of this research, there was no direct evidence of the formation and subsequent repair of MMS-induced DSBs in vivo. This report provides an informational leap in understanding genomic instability.

The investigators treated yeast mutants lacking apn1/2 endonuclease with MMS and detected end-processing of random DSBs using "PFGE-shift," a technique developed in their lab. Since the mutants lacked endonuclease, and were therefore unable to perform base excision repair, the damage led to the creation of apurinic/apyrimidic (AP) sites and subsequently to 3' blocked SSBs. Additional mutations that affected AP sites decreased the number of DSBs. The formation of SMD was independent of resection/recombination processes.

Since approximately 10,000-200,000 SSBs are thought to occur in mammalian cells each day, even a fraction of them turning into DSBs could significantly affect genome stability. These findings provide a greater understanding of the role that DNA damage may play in cancer and cell death.

Citation: Ma W, Westmoreland JW, Gordenin DA, Resnick MA. 2011. Alkylation base damage is converted into repairable double-strand breaks and complex intermediates in G2 cells lacking AP endonuclease. PLoS One 7(4):e1002059.

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Crystal structure-based mutagenesis of EndA nuclease

Investigators at NIEHS, the University of North Carolina at Chapel Hill and Justus-Liebig-University in Giessen, Germany have elucidated the X-ray crystal structure of EndA nuclease at 1.75 Å, and, in doing so, have determined the amino acids involved in its substrate binding and nuclease activity. The study is the first to use site-directed mutagenesis based on structural data to negate DNA binding by EndA nuclease, a member of the ββα-metal finger superfamily. EndA nuclease contributes to the virulence of *Streptococcus* pneumonia, which can cause serious respiratory illnesses. The end goal of this project was to lay the foundation for advances in the production of antimicrobial therapeutics to treat infection.

After determining the crystal structure, the researchers focused on the EndA catalytic site, which exhibited an Asp-Arg-Gly-His motif-containing ββα-metal finger core. Based on their proximity to the nuclease active site, several residues were substituted with alanine to uncover their role in catalysis and binding. These studies identified His154, Gln186, Asn191, Gln192, and Glu205 as being necessary for catalysis, with Asn191 and Glu205 being the most crucial. Additionally, the team found that Arg127/Lys128 and Arg209/Lys210 were necessary for substrate binding.

This study provides an important glimpse into the structure of *S. pneumoniae* EndA nuclease, providing critical information about how it binds the host's DNA. Since EndA nuclease destroys one of the body's defenses against the bacterium, known as neutrophil extracellular traps (NETs), specific inhibitors designed against EndA could help in the treatment of *S. pneumoniae* infection and have significant implications for human health.

Citation: Moon AF, Midon M, Meiss G, Pingoud A, London RE, Pedersen LC. 2011. Structural insights into catalytic and substrate binding mechanisms of the strategic EndA nuclease from *Streptococcus pneumoniae*. Nucleic Acids Res 39(7):2943-2953.

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A novel protective role for beta2 adrenergic receptor in Parkinson's disease

A new research study stemming from a collaboration between researchers from NIEHS and the University of North Carolina at Chapel Hill uncovered a novel protective function for the beta2 adrenergic receptor (beta2AR) in Parkinson's disease. Team members gave mice salmeterol, a beta2AR agonist commercially known as Advair, and found that it protected the rodent brains against inflammation. This effort is the first to show that brain inflammation associated with Parkinson's disease can be effectively decreased using beta2AR agonists.

Chronic neurodegenerative inflammation has been long believed to play a major role in the progression of Parkinson's disease and studies have shown that microglia, the macrophages of the brain, are important mediators of inflammation.

To mimic the symptoms seen in Parkinson's disease, the investigators treated mouse models and neuron-cell glia cultures with the bacterial endotoxin lipopolysaccharide and the neurotoxin MPTP, to cause inflammation associated with Parkinson's. The scientists treated the mice with salmeterol, and saw that even at very low doses (1-10 milligram per kilogram of weight), salmeterol protected the dopaminergic neurons against inflammation. Most importantly, the study further demonstrated that salmeterol reduced the release of pro-inflammatory factors from the microglia.

Although salmeterol and formoterol (Symbicort) are currently being used to treat other inflammatory conditions, such as asthma and chronic obstructive pulmonary disease, they may also be utilized to treat neurodegenerative diseases.

Citation: Qian L, Wu HM, Chen SH, Zhang D, Ali SF, Peterson L, Wilson B, Lu RB, Hong JS, Flood PM. 2011. β2-adrenergic receptor activation prevents rodent dopaminergic neurotoxicity by inhibiting microglia via a novel signaling pathway. J Immunol 186(7):4443-4454.

(Raluca Dumitru, M.D., Ph.D., is an Intramural Research Training Award fellow in the Cell Biology Group of the Laboratory of Molecular Carcinogenesis. Ian Thomas is a writer/editor in the NIEHS Office of Communications and Public Liaison.)

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Inside the Institute

Representative David Price holds town hall at NIEHS

By Eddy Ball

Veteran Congressman David Price, D-N.C., was back in his district June 17 to address NIEHS employees and contractors at a community forum in Rodbell Auditorium. Price represents North Carolina's 4th district, which includes Research Triangle Park and NIEHS, as well as many communities where people who work at NIEHS make their homes and cast their votes.

The forum opened with an introduction by NIEHS Deputy Director Rick Woychik, Ph.D., who said of the guest, "He [Price] is an incredible intellectual and former academic," who earned an undergraduate degree at the University of North Carolina at Chapel Hill and a Bachelors of Divinity, as well as a Ph.D. in political science, at Yale University.

After he entered the auditorium accompanied by NIEHS/NTP Director Linda Birnbaum, Ph.D., Price delivered brief opening remarks in a manner that reflected his ministerial sense of audience and rhythm, as well as his intellectual grasp of the finer points of politics and public policy. He then turned the stage over to his audience for their questions and comments.

"There's nothing in the world that compares to the National Institutes of Health," Price told the audience. "It is a crown jewel in this country." (Photo courtesy of the U.S. House of Representatives)

Few of the participants veered very far away from the budget debates currently underway in both houses of Congress. Price heard concerns about economic stagnation, budget cuts, and their effects on conducting scientific research and recruiting the best minds for the tasks at hand.

Price explained that negotiating the path back to economic recovery will require a spirit of genuine compromise and readiness to sacrifice by everyone involved, to stimulate jobs and investment, as well as erase the deficit and reduce the national debt. "We've got to do two things," he maintained. "The first is to get the economy back to full strength. The second thing we have to do is chart a course to fiscal balance."

Afterwards, Price, center, spoke with individual NIEHS employees. Facing the camera, left to right, are Perry Blackshear, M.D., D.Phil., Rick Woychik, Ph.D., Sheila Newton, Ph.D., and Bill Schrader, Ph.D. (Photo courtesy of Paul Jung)

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"Going local" at the spring Farmers' Fair

By Melissa Kerr

Local farmers and crafters exhibited their produce and products June 15 on the patio outside the Rall Building as part of the NIEHS spring Farmers' Fair. The NIEHS Environmental Awareness Advisory Committee (EAAC) hosted the event to promote the idea of buying local.

"It's very important for us as consumers to reduce our carbon footprint and to know where our food is coming from," explained NIEHS Hazardous Waste Manager and EAAC Co-Chair Paul Johnson.

The abundant spring sun encouraged many NIEHS scientists and staff members to take advantage of the offerings, as well a chance to mingle with friends and colleagues and to take in some people watching.

Fresh flowers and vegetables were available from several different vendors. NTP Research Geneticist Jack Bishop, Ph.D., brought local honey along with a live display of his bees in action. NIEHS Biomedical Engineer Jeff Tucker brought in produce from his farm. Cohen Farms promoted its line of fresh, hormone-free meats and eggs. There was also a display of handcrafted baskets from Rabbit Patch Baskets.

NIEHS Biologist and EAAC member Cindy Innes coordinated the event along with NIEHS Program/Committee Support Assistant Jenn Evans. EAAC member and NTP Health Scientist Diane Spencer also helped with the preparation of the fair. "We were very happy with the response this year," Spencer said.

The EAAC is a committee designed to promote an awareness of the environmental impact of our actions, as well as serving as an advisory body to the NIEHS/NTP director and associate director for management on environmental initiatives.

(Melissa Kerr studies chemistry at North Carolina Central University. She is currently an intern in the NIEHS Office of Communications and Public Liaison.)

Bishop was eager to tell visitors to his table about his bees and their delightful honey. (Photo courtesy of Melissa Kerr)

Like his fellow vendors, NIEHS Biomedical Engineer Jeff Tucker, owner of Sugar Creek Farm, clearly understood the value of presentation as he spread out his spring garden's bounty. (Photo courtesy of Melissa Kerr)

Nothing can brighten a room more than the colorful flowers showcased by Cut & Carry Bouquets owner Marcia Tice. (Photo courtesy of Melissa Kerr)

NIEHS Visiting Fellow Sindura Ganapathi Ph.D., enjoyed the bright display. (Photo courtesy of Melissa Kerr)

As visitors quickly discover, there was no shortage of fresh produce at several booths. (Photo courtesy of Paul Johnson)

Friends and colleagues Cynthia Radford, left, and Evans, right, took advantage of the fair's offerings. (Photo by Eddy Ball)

Cohen Farm displayed a list of organically produced, hormone- and antibiotic-free beef, pork, and eggs available by order. (Photo courtesy of Melissa Kerr)

This spread represents just a small sample of produce and products offered at the fair. (Photo courtesy of Paul Johnson)

Like NIEHS Grants Financial Analyst Benny Encarnacion, left, most shoppers used vendor-supplied plastic bags to take their produce and craft purchases back to the office. (Photo courtesy of Paul Johnson)

But fair goers also had the option of carrying home their bounty in style with handmade baskets on sale at the event. (Photo courtesy of Paul Johnson)

Farmers' Fair exhibitors

The Farmers' Fair brought together nine local food and crafts producers to show off their offerings to people at NIEHS:

- Coon Rock Farm
- Cohen Farm
- Speckled Bird Farm
- Salem Gardens
- Cut & Carry Bouquets by Marcia Tice
- Rabbit Patch Baskets
- Vesta Toppings
- Saddle Creek Honey by Jack Bishop
- Sugar Creek Farm

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